1916
H46.

Hess

The Scale Influence Of Substituents In Paraffine Monobasic Acids. The Divalent Oxygen Atom.

THE SCALE INFLUENCE OF SUBSTITUENTS IN PARAFFINE MONOBASIC ACIDS. THE DIVALENT OXYGEN ATOM

BY

RAY WASHINGTON HESS

B.A. Morningside College, 1912

M.A. University of Illinois, 1914

THESIS

Submitted in Partial Fulfillment of the Requirements for the Degree of

DOCTOR OF PHILOSOPHY

IN CHEMISTRY

IN

THE GRADUATE SCHOOL

OF THE

UNIVERSITY OF ILLINOIS

1916

1916
H46

UNIVERSITY OF ILLINOIS

THE GRADUATE SCHOOL

May 6, 1916

I HEREBY RECOMMEND THAT THE THESIS PREPARED UNDER MY SUPERVISION BY RAY WASHINGTON HESS

ENTITLED THE SCALE INFLUENCE OF SUBSTITUENTS IN PARAFFINE MONOBASIC ACIDS. THE DIVALENT OXYGEN ATOM.

BE ACCEPTED AS FULFILLING THIS PART OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY

C. G. Derick
In Charge of Thesis

W. A. Noyes.
Head of Department

Recommendation concurred in:*

E. F. Washburn
G. W. Pfaff
Joel A. Sperry 2nd

Committee on Final Examination*

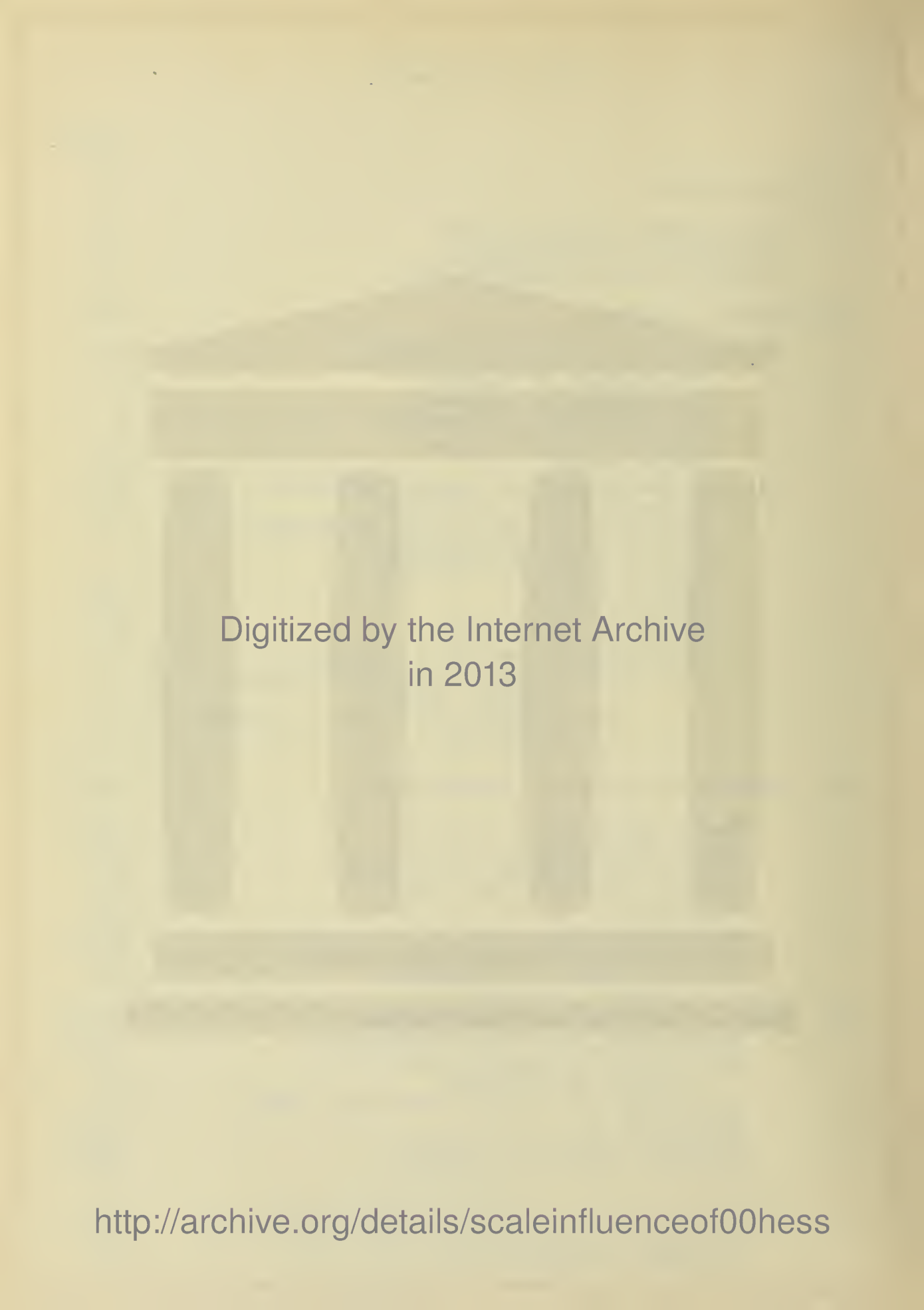
*Required for doctor's degree but not for master's.

343148

Table of Contents.

Table of Contents.

	Pages.
1. Introduction	1-2
Two aspects of the problem	1
Aim of this Investigation.	1
Purpose of the Historical Part	2
11. Chemical Affinity	3-13
1. The nature of chemical affinity	3-6
The element of kinship	3
The element of contrast	3
The mechanical conception	4
Similar to gravitation	4
Modern views	4-5
2. The measurement of chemical affinity	6-13
Affinity tables of Geoffry	6
Bergman, Baume, and Gayton de Morveau	6-7
Contribution of Berthollet	7
Work of Guldberg and Waage	8
Dynamic method	8-9
Static method	9-10
Ostwald, dilution law	10
Thermodynamic measure of affinity	10
Affinities of reactions between perfect gases	12
Affinities of reactions in dilute solutions	13
111. Chemical Affinity and Composition.	14-22
Van't Hoff's generalizations	14-15
Claus and Werner	16
Polarity as measured by Ostwald	16
Views of Vorlander and Abegg	17
Flursheim	18
Bauer and Klages	19
Contribution of Michael and Hibbert	19-20
Derick's measure of polarity	21
1V. Chemical Affinity and Constitution	22-28
Menschutkin, Van't Hoff and Ostwald	22-23
Application of Thiele's theory by Fichter and Pfister	23
Sudborough and Thomas, Derick and Kamm	24
Flursheim	24-25
Michael's scale of influence	25-26
Derick's scale of influence	26-27
V. Chemical Affinity and Space Configuration	28-29
Ionization constants of geometrical isomers	28
Bethman's crowding idea	29


Digitized by the Internet Archive
in 2013

http://archive.org/details/scaleinfluenceof00hess

	Pages
Vl. Chemical Affinity and Valence	30
Vll. Correlation of Chemical Affinity and Constitution	31-32
Bredig, Ostwald, Bethman, Holleman and Derick., Wegscheider.	
Vlll. Theoretical Treatment of the Results of the Present Investigation	33-40
1. Polarity of elements and radicals	33-37
2. Scale of influence	37
General	37
Scale for Oxygen	38-39
Application of the rule of Fichter and Pfister and Flursheim to the Keto-acids	39-40
lX. Experimental	41-85
A. Synthetical	41-68
1.General apparatus	41-46
Vacuum apparatus and method of distillation	41
Melting points	42
A laboratory method for determining boiling points	42-46
2.Preparation of δ-Acetylvalerianic Acid	46-68
Historical	46-47
Trimethylene glycol	47
Trimethylene bromide	48
Historical	48
Method 1	48-50
Method 11	50-51
γ-Bromobutyronitrile	51a-55
Historical	51a
Method 1	52-53
Method 11	54-55
Conclusion	55
γ-Cyano-α-acetylvalerianic ethyl ester	55
Reactions	55-56
Experiment 1	56
Experiment 11	58
Experiment 111	59
Experiment 1V	59
Properties	60
Conclusion	61
1,7-Dicyano 4-aceto 4-carboxethyl heptane	61
Characterization	61-63
Properties	63
δ-Acetylvalerianic Acid	63
Preparation	63-64
Distillation	64
Preparation of the Sodium Salt	65
Recovery of acid from the salt	67

		Pages
IX.	Experimental	43-85
	Titration with $Ba(OH)_2$ solution	67
	Properties of δ-acetylvalerianic acid	68
	B. Conductance Measurements	68-85
	1. Apparatus	69-71
	2. Preparation of Conductivity water	71-72
	3. Water correction	72-73
	4. Preparation of solutions and procedure of measurements	73-74
	5. Conductance measurements and ionization constant of δ-acetylvalerianic acid	75-77
	6. Equivalent conductance at infinite dilution	78-81
	7. The criterion "Calculated Λ_0" applied to the conductance data of δ-acetyl-valerianic acid	81-83
	8. The effect of errors in Λ, bridge reading, resistance box and Λ_0 on the ionization constant	83-85
X.	General Conclusion	86-87
XI.	Summary	88-89
XII.	Bibliography	90

Aknowledgment.

This investigation was undertaken at the suggestion and under the direction of Professor C. G. Derick.

The writer wishes to express his gratitude to Professor Derick not only for his personal interest and helpful suggestions in this work but also for the privilege of working with a man of intense enthusiasm and sincerity as a teacher and an investigator.

R. W. Hess

1 - Introduction.

1- Introduction.

This problem which has been under investigation in this laboratory for the past several years has two important aspects, the one for science in general, that of the influence of an atom or group of atoms upon the strength of the union by which an atom is held within the molecule and the other, one of especial interest to organic chemistry, a correlation of ionization and structure. The nature and measurement of the affinity of the elements for each other was a matter of speculation with the ancient philosophers. At first affinity was thought to be a constant quantity, characteristic of a given element but we are finding it to be a function of more and more variables. The study of the ways by which it is modified is distinctly a modern problem. That there is some relationship between this property and valence and the explanation of the nature of chemical reactions is unquestionable but as yet no definite quantitative relationships have been developed. The correlation of ionization with structure has received some attention but has not been thoroughly studied.

This investigation was undertaken not only with the aim of preparing some d-acetylvalerianic acid and obtaining its ionization constant as a contribution to this bigger problem, but of studying the mechanism of the various reactions involved in its preparation, the regulation of the conditions for producing the best yield of each substance and of characterizing each product found as accurately as possible under the limitations of time and means

at hand. The justification for this is obvious in the light of the trend and requirements in the field of modern organic chemistry.

The historical part is presented with the idea that it should lend appreciation for the difficulties involved and to make obvious the necessity for further investigation. An attempt is made to present the historical evolution of the problem.

1 - V111. Historical and Theoterical.

11 - Chemical Affinity.

The Nature of Chemical Affinity.

As to be expected the first ideas of chemical affinity were in relation to substances rather than atoms, since the atomic theory had not been developed. However, the ancients did notice that when certain substances were brought together they combined, while other substances had no effect upon each other. The idea of affinity was early developed but did not have a generally accepted meaning.

There was one group of ancient philosophers who compared these phenomena to the love and hate of man. To them the term affinity contained the element of kinship. Substances which united had something in common. This idea seems to have been the basis of most alchemical writings. Even in the middle of the seventeenth century Glauber said that lime and smithsonite loved and were loved by acids.

During this same period, 500 B.C., Heracleitos enunciated that the affinity of substances for each other contained the element of contrast rather than that of likeness. It was based upon the principle that unlikes attract and likes repel. This same idea several centuries later found expression through Avagadro, Graham, Brodie and especially the electrochemical theory of Berzelius. During the first part of the 19th century this theory was most generally recognized. Although it fell into disrepute during the following period the essence of the theory is generally recognized at present.

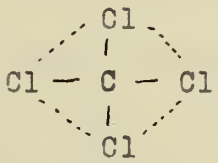
Simultaneously with these other two views, Leucippus, 500 B.C., Democritus, 400 B.C., and Epicurus, 300 B.C., developed the purely mechanical ideas of affinity. According to this conception the particles of matter were held together by minute hooks and points. This conception again found expression and elaboration in the latter part of the 17th century by Lemery. Acids felt as if they were composed of small sharp particles. Since they attacked metals with different degrees of avidity they must have various degrees of sharpness. The particles of alkalies were round and smooth and of such a nature they could be easily penetrated by these sharp points.

With the discovery of the law of gravitation the nature of chemical affinity received an entirely new interpretation. Newton explained affinity as the result of attractions between very minute particles acting at an insensible distance. To Berthollet, chemical affinity was a force identical with gravity, the effect being dependent on the shape and size of the molecules.

Even at the present time the conception as to the exact nature of affinity is hardly less vague than it was to the ancients. A few generalizations are recognized however. To quote Nernst "The force which binds the atoms in molecular union we call chemical affinity of the atom. To the action of this force we must primarily ascribe the fact that the properties of the atom vary so much according to the molecular compound to which they belong and that their properties in the compound are commonly so different from their properties in the free state. This affinity is active in certain directions, the number of these

directions or rays corresponds to the chemical value of the valence of the atom." It is evident that these forces act only in the immediate neighborhood of the atoms and decrease very rapidly with increasing distance from the atom. It is further evident that they vary greatly with the nature of the atom, and for a given atom it depends upon its environment, the temperature, and the solvent. It is especially noticeable in organic substances that the strength of the union by which a given atom is linked varies with the nature and the number of other atoms present within the molecule.

One question which has received less speculation than the others is the manner in which affinity expresses itself. Van't Hoff was the first to recognize an atom to be held not only through the atom to which it is linked but through space to the other atoms in the molecule. For example, carbon tetrachloride might be represented by



where the dotted lines represent the forces of affinity through space or directly. Steric influences also play a certain role that is probably manifested more by the speed by which a given substituent enters a reaction rather than by the force with which it is held within the molecule.

The Measurement of Chemical Affinity.[1]

Although the method for the measurement of these forces of attraction between atoms has been one of slow evolution, it has reached a much more definite state than the conception of its nature. That the situation is not the reverse is fortunate since a knowledge of the strength of chemical affinity and the factors upon which it depends are essential to the solution of valence and the explanation of chemical reactions.

The first attempt to express chemical affinity quantitatively was during the 14th century. It was considered to be a quantity characteristic of a given substance, independent of any variables. If the substance A could give AC from BC then A had the stronger affinity for C, and B could not replace A from AC under any conditions. Obviously the idea of chemical equilibrium was impossible with this conception. Since Cu could replace Ag from its salts and this in turn could be replaced by Pb and Pb by Zn, Zn must have the greatest affinity for acids and Ag the least of these three. As late as 1718 Geoffry[2] formed a table showing the relative affinities of a few substances. Each column contained substances in the order of their affinities for the substance at the head. In 1775 this table was made more complete by Bergman[3] and brought to a more general recognition. He began to realize that affinity, this "Genuine attraction,"

"Free attraction," not a constant for a given substance but considered it to be a function of the temperature only. This idea was first introduced by Baume[4] in 1773, who pointed out that affinities were different at ordinary and at very high tempera-

tures(in wet and dry ways) and that for each substance it would be necessary to construct two tables which should express its behavior under these two sets of conditions.

In 1781 Guyton de Morveau[5] arranged a table whereby double decomposition could be predicted. Each substance was represented by an affinity number. If the affinity sum of the products desired was greater than that for the initial substances a reaction could occur. Thus, since the sum of the affinity numbers of $BaSO_4$ and K-Ac was 92 and that for Ba-Ac and K_2SO_4 was 91 the following reaction would take place,

$$Ba\text{-}Ac + K_2SO_4 \rightarrow BaSO_4 + 2K\text{-}Ac$$

These numbers were obtained empirically and possessed a relative value only. This investigator seemed to realize that temperature, mass, and solubility must have some effect on affinity.

Berthollet[6] especially emphasized and demonstrated experimentally the dependence of affinity,as then considered, on mass. He maintained that if the attraction between atoms obeyed the law of gravitation, the amount of attraction would depend upon the mass of the substance involved. He demonstrated the existence of chemical equilibrium. Because a reaction always went to favor the formation of a gas or an insoluble precipitate he attributed it to the "Elasticität" of the former and the "Kohäsion" of the latter. His difficulties lay in considering total mass instead of concentration. He proposed to measure the affinities of acids by allowing a base to react with equal weights of different acids. His work was further confused by not recog-

nizing the law of constant proportions.

It must be borne in mind that the system of atomic weights and equivalent proportions was not yet clearly enunciated. Necessarily there would be the lack of a unit upon which affinity could be considered.

The classical work of Guldberg and Waage[7] put the problem on its present basis. They demonstrated that the concentration and not the total mass determined affinity. Furthermore their concentrations were expressed in equivalents rather than equal weights. The chemical ehergy then with which two substances act upon each other is the product of the concentration into the affinity coefficient. This latter is a function of the substance, and the temperature.

Dynamic Method for Measuring Affinity.

These methods are used in studying the affinities of acids and bases. It depends upon the relative velocity of saponification by these substances.

Lowenthal and Lenssen[8] in 1862, used the relative velocities of inversion of cane sugar when catalyzed by different acids as a measure of their relative activities. Ostwald[9] developed this work more completely and accurately using the polarimeter to measure the amount of inversion. In the expression

$$k = 1/t \ln A/A-x$$

he called k the inversion coefficient. These values range all the way from 1.114 for HBr to 0.0040 for acetic acid.

Ostwald[10] also studied the rate of saponification of

methyl acetate by different acids using the same equation. The values of these coefficients show the same relative values as in the inversion method.

Likewise a study of the rate of hydrolysis of amides gave approximately the same relative values. In this case the coefficient is,

$$k = 1/t \ .x/A-x$$

since equivalent quantities of acid and amide are used up in the reaction.

The relative affinities of different bases have been studied by Warder[11] and Reicher[12] by the rate of saponification of esters. These values range from 2.307 for sodium hydroxide to 0.011 for ammonium hydroxide.

Static Methods for Measuring Affinity.

This method depends on ascertaining the equilibrium conditions in chemical reactions. If a base was mixed with two different acids the one combined with the larger amount of the base is considered to have the greater affinity for it. Since it was not always possible to obtain an analysis of the system directly, indirect means were often used.

Julius Thompsen[13] used thermal changes for determining the relative affinities of different acids for the same base. Since thermochemical measurements are difficult to make accurately this method has not had extensive application.

Ostwald[14] has correlated changes in volume with the partioning of a base between two acids. In practice the action

of the salt of one acid is allowed to react in solution with an acid and the density taken.

Other less important methods used were the change in optical properties by Jollet, change in specific heat by Pertholet ans Ogier, color changes by Gladstone and the variations of magnetic properties by Wiedemann.

These methods have been generally replaced by an easier and more certain procedure. Pertholett first discovered that the strongest acids were the best conductors of electricity. Then Arrhenius announced the electrolytic dissociation theory upon the basis of which Ostwald's dilution law for weak electrolytes,

$$k = \frac{\alpha^2}{(1-\alpha)\,v}$$

was developed in which k becomes the measure of chemical activity. For strong electrolytes many other equations of an empirical nature have been suggested for expressing the equilibrium conditions

It will be observed that in these methods no attempt is made to express affinity in absolute units. In 1811, previous to the work of Guldberg and Waage, Berzelius[15] proposed to measure the affinity of water for alkali and alkaline earth metals by measuring the vapor pressure at high temperatures. This then could be reduced to absolute units. Later Mitscherlich[16] suggested the same idea for hydrates.

Thermodynamic Measure of Affinity.

As yet nothing is known about the absolute value of the affinities of atoms within the molecule. Thermodynamics, however,

affords a method for measuring the tendency of atoms to enter into chemical reaction, thereby, offering a means for comparing the relative values for the force with which the atoms are held in molecular union. The knowledge of the values for absolute affinities would probably be no more useful.

For many years the magnitude of, ΔU, in the expression,

$$\Delta U = H - W,$$

was considered to be the measure of the tendency of a reaction to occur. This found expression in the Thompsen-Bertholet principle "That every chemical change gives rise to those substances which occasion the greatest development of heat." After a long struggle this theorem was shown to be untenable, Helmholz being one of the principal opponents. Van't Hoff, in 1883, was the first to show that (W) when it became the maximum external work, (A) or "the change in free energy" to be the true measure of affinity.

Evidently the problem is to find the relationship between (A) and some measurable quantities. The most general expression for the free energy of the reaction, between perfect gases or substances in dilute solutions,

$$aA + bB + \ldots\ldots\ldots \rightleftharpoons mM + nN \ldots\ldots\ldots$$

in a homogenous system when carried out reversibly and isothermally at constant volume is,

$$A = RT\ln \frac{C_A^a C_B^b \ldots\ldots}{C_M^m C_N^n \ldots\ldots} + RT\ln \frac{C_M'^m C_N'^n \ldots\ldots}{C_A'^a C_B'^b \ldots\ldots}$$

where C_A etc., is the concentration of the substances which enter into and are removed from the reaction and C_A' their concentration at equilibrium.[17] If each concentration in the first term of the

right hand side of the equation is made equal to unity the expression reduces to,

$$A = R\,T\,\ln K\,,$$

in which K is the mass law constant. From these expressions A, the work gained in the process can be expressed in absolute units. Since K can have any value from an infinitely large quantity to an infinitesimally small one, the maximum work of the process may have theoretically any positive value, any negative value, or zero. In the former case work is gained, in the second case work must be done on the system, while in the latter, work is neither gained or lost.

Affinities of Reaction between Perfect Gases.

For the above expression in its simpler form A is a function of the temperature only for a given reaction between perfect gases. In order to study the affinities between atoms the simplest cases must be considered. In such reactions as,

$$2HI \rightleftarrows H_2 + I_2\,,$$

several unions are involved. Work is required to separate the atoms of I_2 and H_2 but it is gained when they combine to form HI. But in the equilibrium,

$$H + H \rightleftarrows H_2\,,$$

the forces between but two atoms are in play. The maximum work of the process is,

$$RT \ln \frac{(H_2)}{(H)^2}\,.$$

Nernst[18] has calculated the free energy of the reaction

$$C + O_2 \rightleftarrows CO_2$$

and finds it to be 94,000 calories at 1000°.

Affinities of Reactions in Dilute Sokutions.

For reactions in solution, K is evidently a function of the solvent as well as of the temperature. For the ionization of an acid, A, may be considered as a measure of the tendency of the hydrogen ion to form.

Van't Hoff[19] used this expression for the calculation of (A) for several organic acids. Some of the values are given below:

	100k	A
Formic acid	0.0214	2520
Acetic "	0.0018	3280
α-Hydroxypropionic acid	0.0138	2650
β- " "	0.0031	3090
Benzoic acid	0.0060	2900
o-Hydroxybenzoic "	0.102	2050
m- " "	0.0087	2790
p- " "	0.00286	3120
Trichloroacetic "	121.	-60

III - Chemical Affinity and Composition.

Obviously, in a treatment of this kind it is impossible to give a complete review of such an extensive field. To do so would require almost a complete treatise on chemistry since practically all chemical reactions may be resolved into a study of the relationship between chemical affinity, composition, and constitution. In view of this fact merely a brief resume' of the theories of these relationships as applied to organic chemistry will be given.

It is a common observation that the composition of the molecule affects the affinity of the atoms of which it is composed. Thus oxygen increases the acidity of hydrogen sulphide. Sulphurous acid is a much stronger acid than hydrogen sulphide, while sulphuric acid is more strongly dissociated than the former. Likewise sulphur increases the acidity, thiocyanic acid (HCNS) is a stronger acid than hydrocyanic acid(HCN).

Van't Hoff[1] was the first to consider this problem in any kind of a general manner. Speaking of the influence which the introduced element exerts on the behavior of a compound he says, "The introduction has an influence which appears, if in the molecule other linkages can be broken,..... An element communicates its electro-affinity to the atomic group in which it appears and consequently raises or lowers its tendency to associate with positive or negative electricity; commonly the result of this is a more or less positive or negative character in the group. Since we are dealing essentially with organic

compounds carbon is fairly indifferent towards positive or negative electricity, i.e., it shows little tendency to go into the ionic form. Hence the negative or positive influence of associated elements is more completely felt. If this is negative it causes the formation of positive hydrogen ions,i.e., of acid character and reduces the tendency to form hydroxyl ions, i.e., basic character, but only, of course if hydrogen or hydroxyl is contained in the element in question. Positive influence acts in the opposite direction. Hence these opposing influences have first to be dealt with in the case of each element."

He correlates the positivity and negativity of substituents with the state of equilibrium and the velocity of the reactions. He considers the former to be affected mainly by the polarity of the substituent and its position in the molecule while the latter is also a function of steric influence.

He points out that the positive influence of hydrogen is manifested in its removal, producing acidity in acetylene, by the acidity of benzoic acid exceeding that of heptylic acid, and by the greater limits of esterification of hexyl alcohol over that of phenol. The effect of hydrogen upon the rate of reaction is manifested by the fact that with primary alcohols it is greater than in the case of secondary or tertiary alcohols. Likewise the influence of other positive elements,as the light and heavy metals were considered.

The influence of the negative element, as oxygen, chlorine, and nitrogen is shown by their tendency to increase acidity. Further, the speed of oxidation is increased by the presence of oxygen. These are only a few of the many examples

given.

Both Claus[2] and Werner[3] have adopted the view of Van't Hoff that the force with which atoms are linked is not constant but varies with the nature of other elements present. The latter pointed out that substitution on the α-carbon atom in organic acids occurred because the carbonyl oxygen utilized so much of the affinity of the carbon atom to which it is held that but little is left to hold the α-carbon atom leaving a large amount of affinity at this point by which elements attracted.

An attempt to study the relative polar nature of different elements and radicals has been made by Ostwald.[4] Adopting the views of Van't Hoff he considers negative radicals to be those which increase hydrogen ionization while those which decrease the same are classed as positive. Aromatic radicals, hydroxyl, sulphur, halogens, carboxyl, and cyanogen are placed in the former category, while fatty radicals, hydrogen, and the amide groups he places in the latter. His standards for substitution are acetic acid and ammonium hydroxide. The following tables are given in illustration.

		100k	
Acetic acid,	CH_3COOH	0.00180	
-Toluic ",	$C_6H_5CH_2COOH$	0.00556	
Glycollic "	$CH_2OH.COOH$	0.01520	
Thioacetic"	$CH_3.COSH$	0.04690	
Chloracetic	$ClCH_2.COOH$	0.11500	
Malonic "	$CH_2(COOH)COOH$	0.15800	
Cyanacetic"	$CH_2(CN)COOH$	0.37000	
Propionic "	$CH_3.CH_2.COOH$	0.00134	
Glycocol		very small	
	NH_4OH	0.0023	5.23×10^{-5}
	$NH_3(CH_3)OH$	0.0500	
	$NH_3(C_6H_5CH_2)OH$	0.0024	
	$NH_3(C_6H_5)OH$	0.000000011	

From the table it will be observed that sulphur is not

in the same position as the other substituents, so can furnish no idea of its relative negativity. In using ammonium hydroxide, NH_4OH, as a standard the problem is complicated by two sets of equilibria being involved,

$$NH_3 + H_2O \rightleftharpoons NH_4OH,$$

and

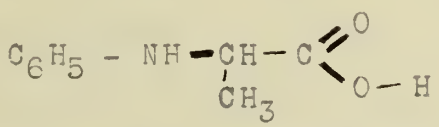
$$NH_4OH \rightleftharpoons NH_4^+ + OH^-,$$

polarity, then, must be calculated in terms of two equilibrium constants since both equilibria will be displaced by the presence of a substituent. Ostwald used neither constant . Thermodynamics will give the relationship.[5]

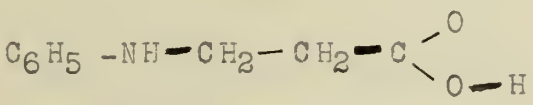
It soon became evident to investigators in this field that affinity is a function of something more than polarity, position, and steric factors. These alone could not explain why anilinoacetic acid is stronger than acetic acid since aniline is a base; why p-hydroxybenzoic acid is weaker than benzoic acid or why o- and p-hydroxycinnamic acids are weaker than cinnamic acid. In order to explain such cases Vorlander[6] says that, "radicals have a double nature, which, on the one hand corresponds to the positive and negative nature of the elements and on the other to the saturated and unsaturated state." Abegg[7] seems to share about the same idea though they are not stated quite as definitely. He correlates the affinity of atoms in compounds with their position in the periodic system. The amount of affinity of atoms for each other as well as its sign depends on the other elements present. Certain elements being amphoteric in character exhibit positive or negative electro affinity depending on the nature of the other elements in the molecule.

Flursheim[8] has shown that the strength of a chemical bond is a function of the disposable amount of chemical force in the atoms which combine, and also the polar nature of that force, and that the rate at which a bond is formed depends partly on both of these factors. In a later article, "The Relation between the Strength of Acids and Bases and the Quantitative Distribution of Affinity in the Molecule," he outlines a qualitative scheme for measuring the three factors, polarity, "the amount of affinity which the linking of a substituent requires, that is the quantitative factor," and steric influences. The first is represented by relative positivity and negativity while the second is conditioned by the saturated and unsaturated state. These factors may support or counteract each other.

In order to explain the above anomalies the "quantitative influence" must predominate. Graphically the following scheme is used.



Flursheim considers C_6H_5NH- to be an unsaturated group, thus requiring a large amount of affinity of the carbon to which it is linked leaving but little for the next and so on. The heavy lines indicate roughly the relative strength of the unions. Since the affinity between the hydroxyl hydrogen and the oxygen is reduced it will permit a greater degree of ionization. Anilinopropionic acid, however, is weaker than acetic acid. In this case we have,



By the same manner he explains why m-chloro, and bromobenzoic acids are stronger than the para isomers.

In order to measure the polarity of radicals he makes use of the expression

$$k_{polar} = \frac{k_{meta} \quad k_{para}}{2k_{benzoic\ acid}}$$

which he maintains eliminates the steric effects and the quantitative factor. The"relative quantitative sequence" is "given as a first approximation," without any definite reason. "The relative sequence of steric effects is approximately known from the rate of acid esterification." Each of these quantities is assigned relative values by the use of (+) and (-) signs and from the combination the result on the ionization constant is predicted. It is extremely qualitative and of questionable value. The effect of substituents upon the course of addition to ethylene linkages has been investigated in several cases.

Bauer[9] has studied the effect of substituents upon the tendency of unsaturated substances to add bromine. Several generalizations are drawn. He agrees with Hinrichsen that negative groups weaken the fourth valency of carbon. The existence of triphenyl methyl is explained in this way.

Klages[10] investigated the reduction of ethylene derivatives. He drew the conclusion that an increase of positive groups on the unsaturated carbons diminished their attraction for hydrogen. Therefore, dimethyl styrene and β-dimethylacrylic acid are reduced with much difficulty.

A large number of papers have been written by Michael[11] on the nature of reactions in organic chemistry. He emphasises

that reactions occur in the direction of the greatest increase of entropy, but estimates this factor only qualitatively. Although all of his terms lack quantitative exactness his scheme is valuable in predicting the cause of chemical reactions. In an article on desmotropism and merotropism he states that the course of a chemical reaction depends on the attainment of a certain "chemical potential." This in turn is determined by two factors "free chemical potential" and the affinity between the reacting atoms. Instead of the word entropy Michael usually substitutes "chemical neutralization." In addition reactions maximum neutralization is attained by the satisfaction of his positive and negative rule. According to this the more electronegative substituents add to the more electropositive part of the molecule and vice versa. Consequently, when HI adds to $CH_3CH = CH_2$, the iodine will join to the second carbon since it is made more positive by the CH_3- radical. At the same time a small amount of $CH_3CH_2CH_2I$, will be formed inorder to satisfy the"distribution principle." According to this principle if ICl is used instead of HI more nearly equal amounts of the two isomeric halides should result, while I-Br should still more nearly equalize the proportions. Experiment confirms this.

Michael interprets the exceptions to Markownikoff[12] rule for the addition of halogen acids to the ethylene union on this basis stating that it involves more fundamental principles.

Hibbert[13] suggests the term "affinergy" instead of Michael's "chemical potential." He proposes to measure the relative affinity of oxygen in ketones by adding differnet members in equivalent quantities to a given hydroxyl compound

and after the use of the Grignard reagent, determine the relative amounts of methane evolved.

Since polarity is generally recognized to be one of the main factors in the influence of one atom upon another, Derick[14] proposes to measure it by the substitution of different radicals for one of the hydrogen atoms of water and gives the following definition:

> "An element or radical possesses positivity if when it is substituted for a hydrogen of water it increases hydroxyl ionization. It is therefore said to be positive.
>
> An element or radical possesses negativity if when it is substituted for a hydrogen of water it increases the hydrogen ionization. It is therefore said to be negative.
>
> In other words a positive radical increases the affinity constant K_b while a negative group increases K_a for water."

For measuring this factor he uses the expression $-\frac{1000}{\log K}$ from the consideration of the free energy function of the ionization constant, RT ln K. By this means he has calculated and tabulated the polarity of a large number of radicals.[15]

Brooks[16] in his discussion on the preparation of acetylchloride makes use of the values of polarity as defined by Derick.

IV - Chemical Affinity and Constitution.

So far the influence of different radicals in the same relative position upon a given atom, and the factors involved, have been considered. The position of a substituent in the molecule has long been recognized as an important factor in the problem of affinity.

Menschutkin[1] was the first to study the problem in a general manner. His investigations were restricted to the limits of esterification and the velocity of attainment of various alcohols with the same acid and different acids with the same alcohol. This study was extended by Bertholet and Gilles.

A little later Van't Hoff[2] pointed out that in general the influence of a substituent decreases with increasing distance between it and the linkage involved. This effect he considered to be expressed through space, "directly" and through the intervening atoms, "indirectly."

Using the ionization constant as the criterion, Ostwald[3] also showed that the nearer the substituent is to the carboxyl the greater the influence upon the affinity constant. Some of the examples given are:

		100k
Propionic acid,	$CH_3.CH_2.COOH$	0.00134
Lactic " ,	$CH_3.CH(OH).COOH$	0.01380
Hydroacrylic" ,	$CH_2(OH).CH_2.COOH$	0.00311
Benzoic " ,	$C_6H_5.COOH$	0.00600
o-Chlorbenzoic",	$Cl.C_6H_4.COOH$	0.13200
m- " ",	$Cl.C_6H_4.COOH$	0.01550
p- " ",	$Cl.C_6H_4.COOH$	0.00930

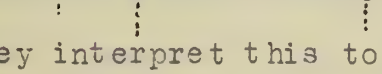
Further, he found that the second substituent in the same position did not produce the same effect on the ionization constant as the first. Other irregularities were observed by Bethmann, Wegscheider, and others especially in the aromatic acids. Since no particular theories were advanced in this connection these will be considered under the correlation of affinity and constitution.

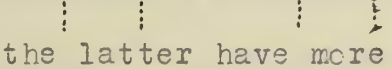
It soon became evident that there were exceptions to this rule. Since the double union is regarded as a negative radical it would be expected to show the same order of influence. Fichter and Pfister[4] pointed out that β,γ-unsaturated aliphatic acids invariably have larger ionization constants than the α,β-acids.

		100k
Crotonic acid,	$CH_3.CH = CH.COOH$	0.00204
Vinylacetic "	$CH_2 = CH.CH_2.COOH$	0.00383
α,β-Pentenoic "	$CH_3.CH_2.CH = CH.COOH$	0.00148
β,γ- " "	$CH_3.CH = CH.CH_2.COOH$	0.00335
α,β-Hexenoic "	$CH_3.CH_2.CH_2.CH = CH.COOH$	0.00189
β,γ- " "	$CH_3.CH_2.CH = CH.CH_2.COOH$	0.00264

Ostwald[5] also showed that the Δ^1 dihydronapthoic acid has a smaller constant than the Δ^2 and the same phenomena is seen in the dihydro-phthalic acids.

Fichter and Pfister have explained this on the basis of Thiele partial valence theory. In the α,β-acids a conjugate system exists while in the β,γ-acids it does not.





They interpret this to mean that the latter have more unsaturation in the molecule, from which it naturally follows they

would be stronger.

In agreement with this Sudborough and Thomas[6] hold that the unsaturation of the β,γ-acids is much greater than that of the α,β-acids since they add bromine so much more readily.

For the dihydronapthoic acids, Derick and Kamm[7] have found the degree of unsaturation, as measured by the free energy of ionization, to be constant for the Δ^2 double union, while that for the Δ^1 double union has been found to vary with the degree of conjugation. They have developed a quantitative interpretation of Thiele partial valence theory for these acids.

Thiele's theory is also an attempt to correlate constitution with the course of addition reactions, especially those of hydrogen. In the conjugate system hydrogen adds to the 1-4 positions rather than the 2-3 positions since there is considered to be more "free affinity" at the former. This theory is criticised by Hinrichsen[8] and Michael[9] on the grounds that it gives too little consideration to the electrochemical nature of the process. They regard it as a special case of a more general principle. On the other hand, Staurt[10] in his book, "Recent Advances in Organic Chemistry" pays the theory many tributes regarding it as one of the most valuable guides in organic chemistry.

Flursheim[11] attempts to explain the irregularities in the "scale of influence" for the double union by the use of his "quantitative factor." He considers this factor to predominate over polarity in this case. The effect is represented graphically by the following unsaturated hexenoic acids.

	100k
$CH_3.CH_2.CH_2.CH_2.CH_2.COOH$	0.00146
$CH_3.CH_2.CH_2.CH=CH-C(=O)-O-H$	0.00189
$CH_3.CH_2.CH=CH-CH_2-C(=O)-O-H$	0.00264
$CH_3.CH=CH-CH_2-CH_2-C(=O)-O-H$	0.00174
$CH_2=CH-CH_2-CH_2-CH_2-C(=O)-O-H$	0.00191

Although Flursheim does not mention it his theory explains why the δ,ε-acid is stronger than the $\gamma\delta$. It might be pointed out here that the rule of Fichter and Pfister does not apply for these two positions.

As pointed out previously, this method is used for explaining why α-anilinepropionic acid is stronger than propionic acid while the β-isomer is weaker.

Since Flursheim places univalent chlorine in the unsaturated group he makes use of this factor to account for m-chloro- and bromobenzoic acids having higher ionization constants than the p-isomers, as well as, a few other anamolies in the aromatic series.

It is not easy to account for the gradual decrease in the ionization constant of an acid according to this theory as many negative substituents are placed in successive portions out the carbon chain, unless the polar factor is assumed to predominate.

In this field again Michael[12] has attempted to explain

a scale of influence. He states that "If we number a certain atom in any fatty compound with a normal carbon chain by the figure 1, our present knowledge of the combined mutual influence between this atom and the others in the molecule is express by the following scale of combined influence, the number indicating the degree of removal and the extent of influence decreasing in the order given, 2-3-5-6-4-7(9-10-11)8. It is to be strongly emphasised that the effect of any atom in position 2 or 3 is far greater than that of any atom less closely connected, and in the case of atoms farther removed, the influence must be largely direct(i.e., spatial)."

It is difficult to see how this scale is derived[13] but the ionization constant seems to be the criterion. Just why Michael considers position 4 to be less important than 5 or 6 is not easily realized in consideration of the relative acidities of glycollaldehyde, $H-\underset{\underset{O}{\|}}{C}-\overset{H}{\underset{H}{C}}-O-H$ and acetic acid, $H-\overset{H}{\underset{H}{C}}-\underset{\underset{O}{\|}}{C}-O-H$.

Derick[14] has made extensive studies on the relationship between affinity and constitution. Using the free energy function as the measure of affinity one of his principal deductions is, "That in open chain compounds possessing normal chains, if the substituent is negative then the scale of combined influen influence for a given negative group in position (1) is 2-3-4-5-6-7-8-9-10-11,etc., i.e., greatest when the negative substituent is in position 2 and decreases proportionallyto the number of carbon atoms intervening. A notable exception to this rule is

that of unsaturated atoms, acids containing the double union."

For measuring the influence he used his "Place Factor",

$$I = \frac{\ln K_o}{\ln K_s} - 1 ,$$

for the above cases the ratio of the place factors for a given substituent in each successive position, approximates a "rule of thirds."

For substituents in the benzene ring[15] he concludes that "no simple relationship exists between the ortho, meta and para place factors for the same radical substituted in bemzoic acid."

Derick has used this same function to explain the course of several reactions. He has shown that intramolecular rearrangements occur only in the direction to decrease the free energy of ionization,[16] and that a knowledge of the value of polarity will enable one to predict the elimination or retention of a molecule of water when aldehydes and ketones are treated with substituted ammonias.[17]

Roth and Stroemer[18] in an article on "Physical Chemical Investigation of the Aromatic Stereoisomeric Acids", in referring to Derick's work on rearrangement state, " Wenige Worte seien einer nicht unwichtigen Arbeit von Derick gewidnet." Henrich[19] in his book, Theorien der Organischen Chemie, makes use of Derick's "Place Factor" in discussing Michael's rule.

V - Chemical Affinity and Space Configuration.

There is recognized to be still another factor besides the nature of the substituent and the number and nature of atoms intervening between it and the atom affected, which plays a role in this problem in many cases. This is manifested by geometrical isomerism and any other factor which may affect space configuration.

Maleic and fumaric acids are composed of the same kind of atoms and the same number of atoms intervene between any two substituents and yet maleic forms an anhydride much easier than fumaric acid. That is, the carboxyl groups have different effects upon each other in the two cases. The same thing may be said of mesaconic and citraconic acids and many others. This, according to Van't Hoff and Wislicenus is due to the relative space positions of the two carboxyl groups as fixed by the double union.

Ostwald[1] found that the ionization constants of the two isomers varied in the same manner. Since he discovered that the nearer a substituent is to the carboxyl group, the greater the effect upon ionization, maleic would be predicted to possess a larger ionization constant than fumaric, if the Van't Hoff-Wislicenus conception is correct. This was actually found to be the case for these two acids, citraconic and mesaconic acids and all acids of this type. That isocrotonic acid is stronger than crotonic acid may be ascribed to the CH_3- radical being positive and its location on the opposite side to the carboxyl. In the case of polycarboxy acids it is known that the ionization is mainly from a single carboxy group. It has been further learned

that the second carboxylic hydrogen ionizes to a greater extent in fumaric than in maleic acid. Ostwald[2] ascribes this to the proximity of the two carboxyl groups, having the same charge, in the latter causing an electrostatic replusion.

Bethman[3] found that the introduction of an alkyl radical into succinic, glutaric acids, etc., invariably raised the degree of dissociation. This is unusual since the alkyl group generally acts in the opposite direction being considered a positive radical. In order to explain this he has given considerable detail to prove that this is due to the radical crowding the two carboxyl groups closer together.

VI - Affinity and Valence.

It is desirable to point out here in a general manner a few ideas of the connection between chemical affinity and valence. Cohen[1] states that, "the term valency is applied to the saturation capacity of one element for other elements and must not be confused with the strength of attachment or chemical affinity; it is a noteworthy fact that the lowest valency is found among those elements in the two end groups of the periodic system which exhibit the greatest affinity." Most scientists seem to agree however, that valence may vary in strength as well as in number. In order to account for the existence of the trivalent carbon atom in triphenylmethyl and divalent nitrogen in N = O Michael[2] concludes that the union of negative radicals produce self saturation. This is not the case in the combination with positive radicals as evidenced by the attempt to prepare CH, CH_2, CH_3, and NH_2, resulting in acetylene, ethylene, ethane, and hydrazine respectively. Michael regards CH_4 as a stable substance because it is neutralized by four positive hydrogen atoms. If the carbon atom is united to an electro-positive metal instead there is a surplus of positivity and a consequent loss of stability, seen in the great chemical reactivity of the metallic alkyles.

There is still another question to be considered in this connection, what effect has the valency of the substituent upon the affinity of the other substituents? But little, if any consideration has been given to this. In a later section this will be treated.

VII - Correlation of Chemical Affinity and Constitution.

Most of the work in this field has been on the correlation of affinity constants of organic acids with chemical constitution. Ostwald[1] was the first to study this in an extensive manner. He studied substitution in both aromatic and aliphatic acids. The ionization constant of the substituted acid divided by that of the unsubstituted acid he called the "Place Factor." By this means it was often found possible to calculate the ionization constants of polysubstituted acids. Ostwald observed that deviation was greatest when the other substituents were on or near the same carbon atom as the first.

Bethman[2] used the Ostwald factor for calculating the ionization constants of several substituted benzoic acids. The agreement with the observed values was fairly good.

Holleman[3] and de Brun also used this factor for calculating polysubstituted acids. They found the greatest divergence was caused was caused by the 1,2,3, acids and that the amount of divergence depends on the value of the substituents.

Wegscheider[4] calculated a large number of these factors for substituents in both monobasic fatty and aromatic acids. In general he found that the greatest deviation between the calculated and observed values when several radicals were on the same carbon atom, for alkyl substituted acids and for the disubstituted aromatic acids when the groups were in positions 1,2,6 or 1,2,3. He also worked out a correlation for substituted and unsubstituted polybasic acids.

Bredig[5] has measured the conductivities of a large number of organic bases, but his ionization constants were not the true values since he did not consider the other equilibria involved.

Derick[6] has used his "Place Influence" $\frac{\log K_o}{\log K_n} - 1$ in his study for both aliphatic and aromatic acids. The advantage of this over the Ostwald factor is that it is necessary to know only the α-influence for a given negative monovalent, substituent in a monobasic paraffine acid in order to calculate the approximate ionization constant for an acid with that substituent in any position. Furthermore, it is necessary to know only the α-factor and the ionization constant of the substituted acid in order to calculate the position of the substituent. He found that these regularities do not exist for the substituted aromatic acids.

VIII - Theoretical Treatment of the Results of the Present Investigation.

1. Polarity of Elements and Radicals.

Radicals which cause hydrogen ionization have been defined as negative while those which decrease the same have been defined as positive. It has been observed, however, that some radicals do not act uniformly, consequently it is difficult to determine their polarity. It is obvious that for practical purposes the knowledge of the polarity of these radicals would be of but little value since it is of such feeble character. On the other hand, there are many radicals which always act uniformly in the direction of their effect, if not in exact numerical value. Consequently, the knowledge of the values of their polarities should be very useful in this problem.

The first question is as to the proper standard into which radicals may be substituted. Investigators disagree on this. As previously mentioned Ostwald used acetic acid while Derick adopted the neutral molecule of water.

For the present purpose any monobasic paraffine acid may be used since radicals with pronounced polarity act uniformly when substituted. Acetic acid has been chosen for calculating the values in table 1.

The next question is in regard to the correct manner of measuring polarity. Since in practical cases we wish to know the effect of a substituent upon the tendency of a given atom to enter into a chemical reaction, it is obvious that polarity must be measured in terms of this tendency if it is to be of any

service. Neither the algebraic value of the ionization constant nor the degree of ionization may be used for this purpose.

As Van't Hoff[1] pointed out, when an acid is changed from unit concentration of its ions to unit concentration of unionized molecules, the free energy of the process is,

$$A = -R\,T\,\ln K\ ,$$

where K is the ionization constant. If a substituent is introduced into a given acid the value of A will be changed since it will affect K. Obviously, the change in this value due to the substituent may be calculated from the expression,

$$I_s = -R\,T\,\ln K_n - (-RT\,\ln K_o),$$

where K_n is the ionization constant of the substituted acid and K_o that for the unsubstituted acid. This, of course, neglects the influence of the removal of a single hydrogen atom, which Derick[2] has shown to be negligible. Since both constants must be determined at the same temperature this expression reduces to,

$$I_s = 2.303\,RT\,(\log_{10} K_o - \log_{10} K_n),$$

If a substituent increases the ionization of the acid, I_s will be negative while if it decreases the same, the quantity will be positive. From this it follows that negative values and their magnitudes will represent relative negative polarity while positive values and their magnitudes will express relative positive polarity when different substituents are placed in the same position in an acid which obeys the mass law. If relative values

only are desired, the expression,

$$\text{Polarity} = \log_{10} K_o - \log_{10} K_n ,$$

will be simpler and more useful.

The negative quantities in the last column of table 1 are relative values of the work that must be done in order to repress the tendency of the carboxylic hydrogen to ionize due to the substituent, while the positive numbers are the relative values of the work gained in the repression of the ionization due to the substituents.

Relative Polarity of Radicals.

Table 1

Acid	K_a	log $K_a^{25^o}$	Radical	Polarity
$CH_3NH.CH_2.COOH$.....	1.2×10^{-10}	-9.920	$CH_3.NH-$	5.19 (?)
$(CH_3)_2N.CH_2.COOH$..	1.3×10^{-10}	-9.880	$(CH_3)_2N-$	5.15 "
$NH_2.CH_2.COOH$.....	1.8×10^{-10}	-9.740	NH_2-	5.010 "
$CH_3CH_2.COOH$.....	1.45×10^{-5}	-4.839	H_3C-	0.107
$CH_3.COOH$.....	1.85×10^{-5}	-4.733		0.000
$C_6H_5.CH_2CH_2.COOH$...	2.30×10^{-5}	-4.650	$C_6H_5CH_2-$	-0.085
$C_6H_5.CH_2.COOH$.....	5.02×10^{-5}	-4.299	C_6H_5-	-0.434
$CH_2(OH).COOH$.....	1.50×10^{-4}	-3.820	$HO-$	-0.910
$C_2H_5OCH_2.COOH$.....	2.34×10^{-4}	-3.630	C_2H_5O-	-1.100
$CH_3OCH_2.COOH$.....	3.00×10^{-4}	-3.520	CH_3O-	-1.210
$CH_2(COOC_2H_5)COOH$...	4.51×10^{-4}	-3.350	C_2H_5OOC-	-1.390
$I.CH_2.COOH$.....	7.50×10^{-3}	-3.120	$I-$	-1.610
$Cl.CH_2.COOH$.....	1.55×10^{-3}	-2.810	$Cl-$	-1.920
$Br.CH.COOH$.....	1.38×10^{-3}	-2.860	$Br-$	-1.870
$CH_3.CH_2.COOH$.....	1.41×10^{-5}	-4.850	-	-
$CH_3.CO.COOH$.....	3.67×10^{-3}	-2.43	$O=$	-2.420

The values given for the polarity of the amino groups in table 1 are not corrected since some of the molecules will have hydrolyzed to give such radicals as $-NH_3$ and $-NH\,CH_3$ so that it is the resultant effect of these groups plus NH_2- and $NH.CH_3-$ that is measured. The probelm is further complicated by the repression

of the hydrogen ionization due to the accumulation of hydroxyl ions from the hydrolysis. These values were calculated merely as an illustration of the method.

The reason for using propionic acid for obtaining the polarity of oxygen is that glyoxylic acid is not known in the dehydrated state. The same value should be obtained since the influence of all the other atoms is eliminated in any case. This is shown in the following table where the polarities of chlorine and bromine are calculated when substituted into acetic, propionic and butyric acids.

Table II

Acid	$K \times 10^{-3}$	log K	Polarity
Chloracetic acid.....	1.55	-2.81	-1.92
α-Chloropropionic ".....	1.47	-2.83	-2.02
α-Chlorobutyric ".....	1.39	-2.86	-1.95
Bromoacetic acid.....	1.38	-2.86	-1.87
α-Bromopropionic ".....	1.08	-2.97	-1.88
α-Bromobutyric ".....	1.06	-2.98	-1.82
	$K \times 10^{-5}$		
Acetic acid.....	1.85	-4.73	
Propionic "	1.41	-4.85	
Butyric "	1.56	-4.81	

It should be observed that when two or more radicals with marked polarity are present within the same molecule the polarity of each is modified.

Table III

Acids.	K	log K	Polarity
$CH_3.COOH$	1.85×10^{-5}	-4.73	
$CH_2.Cl.COOH$.....	1.55×10^{-3}	-2.81	-1.92
$CH.Cl_2.COOH$.....	5.14×10^{-2}	-1.29	-1.52
$C.Cl_3.COOH$.....	1.20 (?)	0.079	-2.08

The introduction of the second chlorine atom is seen to have less effect than iodine or bromine while in the paraffine acids it has greater influence than either.

Likewise, deviations are shown by the hydroxy-substituted propionic acids.

Table IV

Acids	K	log K	Polarity(OH)
$CH_3.CH_2.COOH$.....	1.41×10^{-5}	-4.85	
$CH_3.CHOH.COOH$....	1.38×10^{-4}	-3.86	-0.99
$CH_2.OHCH_2.COOH$...	3.10×10^{-5}	-4.51	
$CH_2.OH.CHOH.COOH$.	2.00×10^{-4}	-3.70	-0.81

2. Scale of Influence.- General.

After having gained some idea of relative effects of different substituents in the same position, it becomes of interest to determine the modifications of distance. Using the same expression, $\log K_o - \log K_n$, this may be calculated. Table V makes it evident that the effect of the substituents upon the tendency of hydrogen to ionize is less in each successive position to the α-carbon in the monobasic paraffine acids.

Table V

Acid	K	log K	Position	Polarity
Chlorine.				
$CH_2.Cl.COOH$.....	1.55×10^{-3}	-2.81	α	-1.920
$CH_2.Cl.CH_2COOH$.....	8.59×10^{-5}	-4.07	β	-0.773
$CH_2.Cl.(CH_2)_2COOH$..	3.00×10^{-5}	-4.52	γ	-0.281
$CH_2.Cl.(CH_2)_3COOH$..	2.04×10^{-5}	-4.69	δ	-0.107
Bromine.				
$CH_2.Br.COOH$.....	1.38×10^{-3}	-2.86	α	-1.870
$CH_2.Br.CH_2COOH$.....	9.80×10^{-5}	-4.00	β	-0.820
$CH_2.Br.(CH_2)_2COOH$..	2.60×10^{-5}	-4.50	γ	-0.210
$CH_2.Br.(CH_2)_3COOH$..	1.91×10^{-5}	-4.72	δ	-0.079

Table V (con't)

Acids	K	log K	Position	Polarity
Hydroxyl.				
$CH_3.CH(OH).COOH$....	1.38×10^{-4}	-3.86	α	-0.970
$CH_2(OH).CH_2.COOH$...	3.10×10^{-5}	-4.50	β	-0.330
$CH_2(OH)(CH_2)_2COOH$.....	1.93×10^{-5}	-4.71	γ	-0.092

Scale of Influence for Oxygen.

Up to the present there has been no data available for calculating the influence of a substituent in the ε- and ζ- positions. The purpose of the present investigation was to determine the influence of a radical in the ε-position. The other case has been treated by Derick and Brady.[3] The scale of influence for oxygen follows:

Table VI

Acid	K	Position	$\frac{K_n}{K_o}$	$\frac{\log k_o}{\log k_n} - 1$	$\ln K_o - \ln K_n$
$CH_3.CO.COOH$.....3.67×10^{-3}		α	260.0	0.9920	-2.410
$CH_3.CO(CH_2)COOH$.. 1.50×10^{-5}		β	24.5	0.3630	-1.390
$CH_3.CO(CH_2)_2COOH$....2.405×10^{-5}		γ	1.59	0.0435	-0.201
$CH_3.CO(CH_2)_3COOH$....2.295×10^{-5}		δ	1.58	0.0430	-0.198
$CH_3.CO(CH_2)_4COOH$....1.930×10^{-5}		ε	1.33	0.0262	-0.124
$CH_3.CO(CH_2)_5COOH$....1.638×10^{-5}		ζ	1.14	0.0117	-0.053

The following values of the ionization constants for the unsubstituted acids were used.

Table VII

Acids	K x 10^{-5}	log K
$CH_3.CH_2.COOH$	1.41	-4.850
$CH_3(CH_2)_2COOH$		
$CH_3(CH_2)_3COOH$	1.51	-4.821
$CH_3(CH_2)_4COOH$	1.45	-4.838
$CH_3(CH_2)_5COOH$	1.45	-4.838
$CH_3(CH_2)_6COOH$	1.44	-4.838

Column 3 gives the Ostwald Factor. From column 4 it is evident that oxygen does not follow the rule of thirds. It has been observed that all monovalent negative radicals approximate this rule. In this case the deviation may be due to the divalency of the element. It will be necessary to study this further by substituting other polyvalent elements. Since unsaturation has been found to be a factor in irregularity in some cases it may play a role in this case. It was thought that this might be due to hydration on the ketone oxygen but Derick and Brady have shown that this is not very probable.[4] Column 5 shows that the influence is less in each succeeding position. The scale of influence of oxygen upon the tendency of hydrogen to ionize has been tested and found not to have the order suggested by Michael 1-2-3-5-6-4-7(9-10-11)8 but 1-2-3-4-5-6-7-8-9-10-11, as given by Derick.

One surprising feature of this investigation is that the influence of oxygen in the γ-, and δ-positions appears to be about the same. It is difficult to explain this with our present knowledge of the problem. Before much theorizing is attempted the influence of monovalent radicals in the ε-, and ζ-positions as well as that of the other polyvalent radicals should be determined.

It is of interest to apply the rule of Fichter and Pfister to the keto acids. In pyroracemic acid, $CH_3.\overset{\delta}{C}.\overset{\gamma}{C}.OH$, there should be less unsaturation than in acetoacetic acid, $CH_3.\overset{\beta}{C}.CH_2.\overset{\alpha}{C}.OH$. If there were no other variables acetoacetic acid should be stronger, but it has been shown to be weaker(see table VI). In this case the distance of the oxygen may be a

greater factor than the unsaturation. Since the above rule was derived for carbon to carbon unsaturation the polarity of the hydrogen will be but a small factor. On the other hand, the fact that acetoacetic acid is so much less stable than pyroracemic indicates that the former is more negatively substituted since negative substitution decreases the stability of the carbon to carbon linkage. The value given for the strength of this acid may be in error. This consideration points out the limitations of the theory.

Of course, strictly, the comparison should be made between acetoacetic acid and propioacetic acid but that CH_3- group will have but little effect in comparison to the other factors in this case, is generally recognized. At any rate this may be eliminated by comparing the free energy function, ($\log K_o - \log K_n$) in the two cases. (See table VI).

The limitations of Flursheim's theory is evidenced by the attempt to apply it to these keto acids. If his "quantitative factor" predominates here as in the case of the unsaturated acids pyroracemic acid, $CH_3.C(=O)-C(=O)-O-H$ should be a weaker acid than propionic acid, $CH_3.CH_2.COOH$, and levulinic acid, $CH_3.C(=O)-CH_2-CH_2-C(=O)-O-H$ should be weaker than butyric acid, $CH_3.CH_2CH_2CH_2COOH$, but the reverse is true. If we are to accept this theory the polar and steric factors must be considered to predominate.

1X - Experimental.

A. Synthetical.

1 - General Apparatus.

Vacuum Apparatus and Method of Distillation.

Since most of the separation and purification of material was effected by fractional vacuum distillation a brief description of the general apparatus used will be given.

For producing and maintaining a vacuum a May-Nelson rotary pump was used. By having a T tube with a pinch cock in the system the vacuum could be controlled and kept anywhere with in the limits of a few tenths of 1 mm to 760 mm. It was not necessary to have a fractionating receiver since the vacuum could be broken and a new receiver connected and a vacuum produced again within a few seconds. Another advantage of using this pump is that it prevents having water saturated air in contact with the distillate in cases where it would be undesirable. It was found necessary to introduce hard oil at the suction intake frequently in order to maintain the efficiency of the pump.

For distillation flasks the Claissen type with the side tube joined by a large connection was used. Ordinary distillation flasks were used for receivers.

In order to eliminate superheating as much as possible, besides the capillary tube a few small pieces of porous plate were placed in the flask and the surface of the liquid was not allowed to stand below the surface of the bath.

For heating the liquid the flask was immersed in a Wood's metal bath, the temperature of which was followed by inserting a

thermometer.

For the final distillation Anschutz thermometers were used

The aperatures were generally closed by means of rubber stoppers, though in some cases ordinary corks covered with sealing wax were considered to be better.

2. Melting Points.

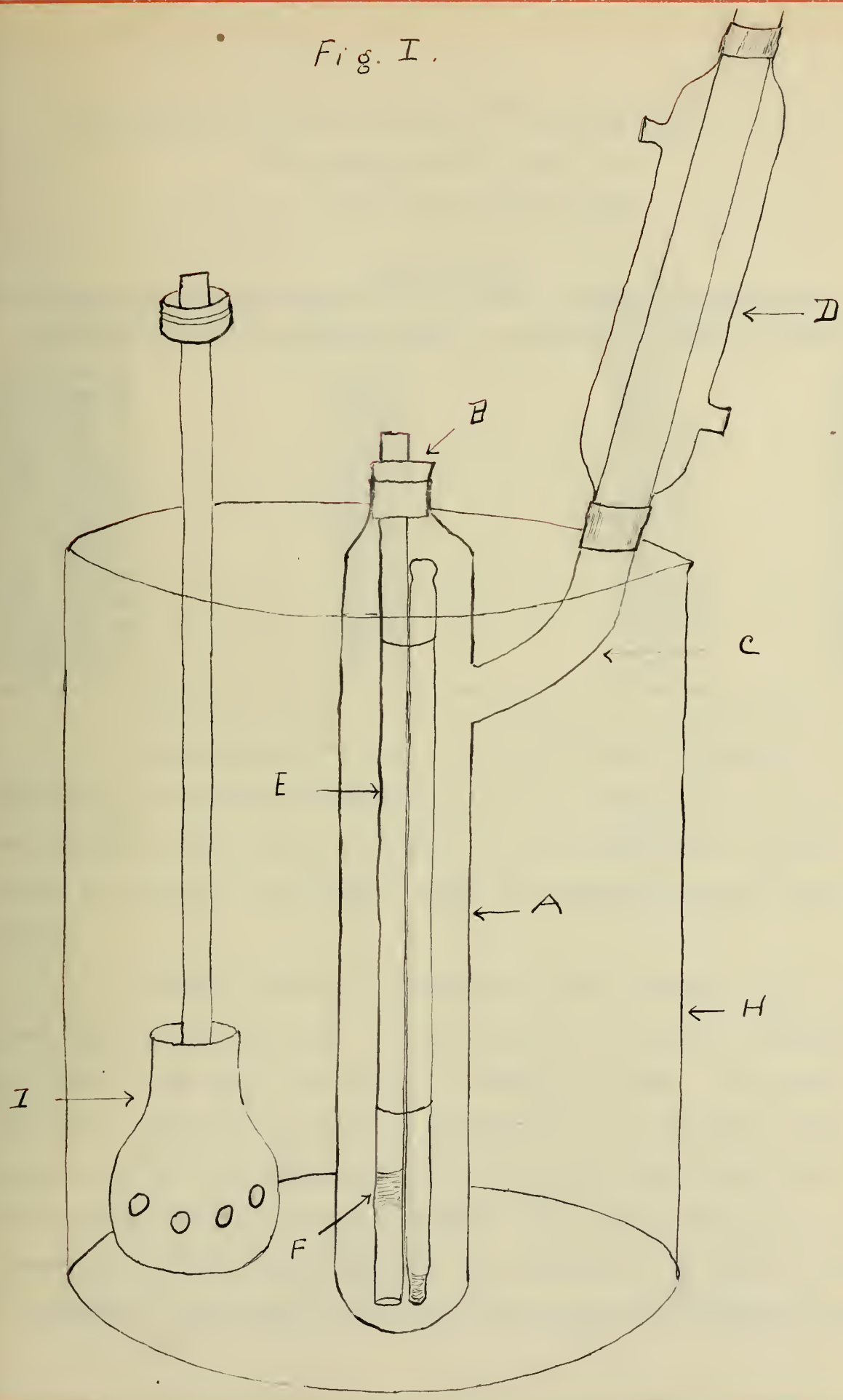
Melting points were taken by the capillary tube method.

3. A laboratory Method for the Determination of Boiling Points.

Since it was found that in many cases the temperature of vacuum distillation, even though every precaution was taken to prevent superheating, depends on the temperature of the bath and the rate of distillation, the study of a practical laboratory method for obtaining boiling points accurately and for standardizing thermometers was undertaken. The principle was essentially that of the equilibrium method frequently used in this laboratory, but the apparatus was modified in several respects. The reproducibility of the method to an accuracy of 0.2° was first studied using Anschutz thermometers by observing the boiling point of water as indicated under different modifications of the apparatus. The thermometer was placed in the water instead of the bath. It was found that the boiling point tube could not be used as a condenser since the condensate on coming in contact with the cavity at the lower end of the tube would cool this by causing the vapor within to condense while the temperature of the liquid was higher than the boiling point of the water, the amount of variation not always being the same. For the same reason it was found best to keep the temperature of the entire tube uniform.

In order to facilitate this without loss of vapor a condenser was connected by means of a side tube. The apparatus, Fig. 1, as finally found to give the best results consisted in a jacket (A) of 22 mm internal diameter and 190 mm in length narrowed at the top top in order to prevent any unnecessary exposure of the surface of the stopper(B). Near the top of this a side tube (C) of 7 mm internal diameter bent upwards, surrounded by a small condenser jacket (D). Through the stopper a hollow boiling point tube (E), closed at (F) about 2/3 of an inch from the lower end, was inserted To this an Anschutz thermometer was attached by means of platinum wire, so that its bulb was even with the end of the tube. The outside jacket was surrounded completely with a two liter beaker (H) containing concentrated sulphuric acid, heated by means of a gas burner. The stirrer (I) was run by a small electric motor. By the use of this large bath it was easy to maintain equilibrium conditions. For obtaining a boiling point the lower end of the tube and the thermometer was placed nearly to the bottom of the jacket and enough water added so that the cavity below (F) is about half immersed at equilibrium. It was found necessary to slightly superheat the water and then allow the temperature to slowly drop.until the level of the liquid in the cavity just passed, that in the jacket,at which point the temperature was read. When the proper temperature was reached the tube sometimes required gentle tapping in order to start the bubbling. The reproducibility of the boiling point with this apparatus is given in table VIII.

Fig. I.



Reproducibility of steam Point Determination.

Barometer Reading 750.8 mm

Room Temperature 21.5°

Table VIII

	Temperature of water		Temperature of bath	
	Initial ± 0.1°	Final ± 0.1°	Initial ± 0.5°	Final ± 0.5°
(1)	100.5°	100.4°	104°	102°
(2)	100.6°	99.8°	104°	102°
(3)	100.2°	100.0°	103°	102°
(4)	100.1°	99.8°	103.5°	102°
(5)	101.0°	99.8°	105.0°	102°
(6)	100.6°	100.0°	104.5°	102°
(7)	101.0°	100.3°	106.0°	103°
		99.8°		102°
(8)	100.5°	99.9°	104.0°	102°
(9)	101.0°	99.8°	105.0°	102°
(10)	100.7°	99.8°	105.0°	102°
(11)	100.7°	99.8°	104.5°	102°
(12)	100.9°	99.8°	105.0°	102°

The thermometer used in the bath was not checked against the Anschutz thermometer. In (7) although the liquid receded into the cavity at 100.3° it was pushed back and remained level with that in the jacket until the temperature had dropped to 99.8°.

Whether constant superheating was present or not in this case has not been rigidly investigated but since this thermometer is known to be fairly accurate it cannot be great. In order to complete this study it will be necessary to investigate superheating as well as reproducibility for many other substances at ordinary and under reduced pressure. For this purpose it will be necessary to know accurately the boiling points of these substances. A search of literature has shown that especially for the higher

boiling substances there is considerable divergence of the values given.

If the method proves to be accurate it will be possible to determine the boiling point of a substance under various pressures with a relatively small amount of material and within a short time by attaching a controlled vacuum at the end of the condenser.

2 - Preparation of δ-Acetylvalerianic Acid.

Historical.

δ-Acetylvalerianic acid has been obtained by several investigators but the yield was small and the purity questionable in most cases.

W. H. Perkin[1] was the first to have prepared this substance. The method consisted in condensing two moles of acetoacetic ester with one of ethylene bromide forming αα,-diacetyladipic ethyl ester, which was partially saponified by dilute alkali to α-diacetylvalerianic ethyl ester. This was further saponified by strong alkali to the desired product. The yield was not stated. The melting point was given at 40-42° and the boiling point 250-253° at 280 mm. It was found to be soluble in organic solvents. With phenylhydrazine it formed an oily precipitate.

Fichter and Gully[2] merely state that α-acetyladipic ester, formed by the condensation of acetoacetic ester with γ-chlorobutyric ester, saponified by the ketone decomposition gives δ-acetylvalerianic acid.

In the characterization of 1,2, methylcyclohexanone,

Wallach[3] states that it is oxidized to δ-acetylvalerianic acid by chromic acid. The semi-carbizone, m.p., 144-146° was prepared and the acid regenerated. The melting point was given at about 50°. At another time it was impossible to regenerate the acid which would crystallize, Wallach thought that tautomerism or hydration might be interfering. Later this investigator[4] found that it was one of the oxidation products of 4 cyclohexene acetic acid. The product was found to melt at 38-40° and quickly liquified when exposed to moist air.

Blaise and Koehler[5] reported an excellent yield of this acid from the action of $CH_3.Zn.I$ on the half ester acid chloride of adipic acid. The melting point is given at 31-32°. No other properties are described.

The following method has not been used for preparing δ-acetylvalerianic acid before. It consists in making trimethylene bromide from trimethylene glycol, the conversion of this to the brom nitrile, its condensation with acetoacetic ester forming δ-cyano-α-acetylvalerianic ethyl ester and the hydrolysis of this to δ-acetylvalerianic acid. It was found that this substance, prepared by other investigators, melted from 30° to 50°. The product prepared by the above method, when pure, melts sharply at 36.5°.

Trimethylene Glycol.

The literature shows that this substance has usually been prepared from trimethylene bromide. It has also been found to be formed by the action of bacteria upon glycerine. It is quoted by

Schuhardt at the fabulous price of 800 marks per kilogram.

The trimethylene glycol used for this synthesis was obtained by the fractional distillation of "Blizzard- Anti-Freeze Compound," sold by the Globe Soap Company of Cincinnati, Ohio, for automoblie radiators. The yield was generally as high as 80-90%.

Trimethylene Bromide.

Historical.

One of the first and the method most generally used for the preparation of this bromide was the action of HBr on allyl bromide. Reboul about 1870,[6] Germont 1871,[7] Erlenmeyer in 1879[8] and others studied the method under varied conditions, in the cold, heated in a bomb, with and without the presence of water, always finding more or less of the isomeric propylene bromide produced also. The disadvantages of the method are obvious.

Later in 1881 Freund[9] treated trimethylene glycol, obtained by the fermemtation of glycerine, with concentrated HBr in a sealed tube at 100° and formed trimethylene bromide. The yield was not stated. The boiling point was found to be 164.5-165.5°. Analysis for bromine was 2% low. It probably contained some γ-brompropyl alcohol.

In a note on the use of Kohlbaum's products Gustavoson[10] redistilled obtained a range of fractions from 140-166°. Most of it decolorized $KMnO_4$ quickly.

The Present Method.

Method 1.

Excellent yields of trimethylene bromide were obtained from

the action of aqueous HBr on trimethylene glycol without the inconveniences of the Freund sealed tube method. The following equilibria,

$$OH(CH_2)_3OH + 2HBr \rightleftharpoons OH(CH_2)_3Br + HBr + H_2O \rightleftharpoons Br(CH_2)_3Br + 2H_2O$$

will be established. The effect of an excess of HBr on displacing the equilibrium to the right has been clearly demonstrated. The technique of the Norris method was first tried but a much better yield was obtained by a simple modification of this. The comparative results follow.

In the first case only a small excess of HBr was used. 300 grams of trimethylene glycol, b.p., 215-216°, was added 1000 cc of constant boiling aqueous HBr in a three liter flask and refluxed over a sand bath for about four hours. The mixture then, was distilled inorder to remove the water and the bromide first, displacing the equilibrium to favor the yield. Three fractions were collected, one from 100-110° and 110-125°, both composed of two layers of about equal volumes and one from 125-160° with but little of the heavier layer. The bromide was separated in each case and added together, dried over $CaCl_2$, filtered and distilled. Upon warming the clear liquid a large amount of $CaCl_2$ separated indicating the presence of an alcohol. Repreated fractionation gave some trimethylene glycol, water, and probably some γ-bromopropyl alcohol. The above equilibrium predicts this. Yield 375 grams boiling at 165°, 47% theoretical. The aqueous layer from the first fraction was discarded, that from the second was redistilled giving a small amount of constant boiling HBr, while

the third fraction distilled almost completely at 125° and was 48% HBr.

Method 11.

The principle of the second method was to reflux one mole of trimethylene glycol with enough constant boiling HBr to furnish three moles of HBr and then to pass in 2 moles more of gaseous HBr. For this purpose the following preparations were used, 400 g. of trimethylene glycol and 1800 cc of constant boiling HBr, placed in a four liter flask. This was refluxed on a sand-bath 3-4 hours and allowed to cool, then 850-900 grams of gaseous HBr were introduced.

The HBr was generated as follows. A large apparatus was used since considerable quantities of the gas is continually used in the laboratory. The apparatus was made up of a four liter flask bearing a two hole stopper through which a dropping funnel and a bent tube were inserted. The latter was connected to a U tube 1.5 inch in diameter and about 12 inches long by means of a cork which also bore a safety tube containing concentrated hydrobromic acid. This U tube was connected to a second of the same size. These were filled with a moistened mixture of red phosphorus and glass wool. The best manner by which to fill these was to mix the glass wool and the phosphorus dry, place loosely in the tubes and run a current of steam through. This prevents the formation of lumps and the stoppage of the tubes by the other method. If the mixture is not wet enough a large amount of a yellow substance is formed during the generation of the HBr. This can be decomposed by a current of steam carefully regulated

producing considerable HBr. For an apparatus of this capacity it was found best to have all connecting tubes not smaller than 0.5 inch in diameter since if the process is carried out rapidly these tubes may become stopped with this yellow deposit if they are smaller than this. A convenient charge was found to be,

1600 grams of sand.
300 cc of water.
200 grams of red phosphorus.
1200 grams of bromine.

The sand, phosphorus and water were mixed intimately and placed in the flask. The bromine was dropped at the desired rate from the funnel onto the mixture. In the present case it required but 2-3 hours to generate the 900 grams of HBr required.

This mixture was gradually brought to boiling and refluxed again for two hours in order to establish equilibrium. Upon cooling, the bromide completely precipitated from the acid solution. This was separated, washed twice with 200-300 cc of water in order to remove any unchanged glycol and twice with 100 cc of cold concentrated sulphuric acid to extract the γ-bromopropyl alcohol. It was further washed with (1-10) sodium carbonate solution until the washings remained alkaline and finally with 200 cc of water and dried with $CaCl_2$ and distilled. It boiled constant at 165°. Yield 870 grams or 82% theoretical as compared to 47% by the other method. A small amount of γ-bromopropyl alcohol may be obtained by pouring the sulphuric acid extract into ice shavings and extracting with ether.

An amount of constant boiling HBr equivalent to the amount used is regained by distilling the aqueous layer.

γ-Promobutyronitrile.

Historical.

Gabriel[11] prepared this substance from trimethylene bromide and potassium cyanide using the ordinary solvent, a mixture of ethyl alcohol and water. Only approximately 40% of the bromide used can be accounted for. The yield of the nitrile was 20-25% of the bromide which has actually disappeared only 10% being recovered. He reports that it boils at 205° with slight evolution of HBr. It was purified by distillation under ordinary pressure.

The main reaction is,

$$Br.CH_2.CH_2.CH_2.Br + KCN \rightarrow Br.CH_2.CH_2.CH_2.CN + KBr$$

$$Br.CH_2.CH_2.CH_2.CN + KCN \rightarrow CN.CH_2.CH_2.CH_2.CN + KBr$$

In aqueous solutions made alkaline by the hydrolysis of potassium cyanide, a large number of hydrolysis products would be expected. This might account for the poor yield. Since potassium cyanide was found to be appreciably soluble in methyl alcohol it was predicted that this used as a solvent would prevent hydrolysis and give better yields. This was found to be true by the following experiments.

The directions of Gabriel were first repeated using the same proportions:

Trimethylene bromide, b.p. 165°	202 grams
Potassium cyanide, Eimer and Amend 98-100%	65 grams
Ethyl alcohol	700 cc
Water	120 cc

To the potassium cyanide solution dissolved in warm water the warm alcohol was added. Kept warm on the steam-bath over night; the alcohol was distilled as completely as possible from the

steam-bath, 150cc of water was added to dissolve the potassium bromide and the oily layer was separated. By repeated fractional distillation the following results were obtained.

Fraction	Tempt.	Pressure	Amount	Substance
1	65-75°	22 mm	15 g	$Br(CH_2)_3Br$
11	105°	22 ..	39 g	$Br(CH_2)_3CN$
111	159°	22 "	14 g	$CN(CH_2)_3CN$

39 gms. $Br(CH_2)_3CN$ = 54 grams $Br(CH_2)_3Br$
14 " $CN(CH^)^CN$ = 30 " "
15 " " remaining
99 " "

The yield of γ-bromobutyronitrile is 28% on the basis of the bromide which has dissapeared, 7.5% being recovered while 15% was converted into trimethylene cyanide, thus accounting only for one-half of the trimethylene bromide. These results are but little better than those of Gabriel. The aqueous layer was found to turn congo red paper blue proving the presence of a strong acid. The odor of the isonitrile was very noticeable both in the alcoholic distillate and in the aqueous residue.

Method 1.

One manner in which the new method was tried was to add the potassium cyanide in several portions at intervals during the refluxing in order to prevent the potassium bromide from precipitating onto the potassium cyanide hindering its dissolution. One mole of potassium cyanide was used to one mole of the bromide.

Materials.		
	$Br(CH_2)_3Br$	435 grams.
	KCN	140 "
	CH_3OH	1300 cc

The bromide was prepared pure as described previouly, b.p. 165°. The potassium cyanide was that of Eimer and Amend labeled, 98-100%. Methyl alcohol bearing the Eimer and Amend brand was refluxed over

250 grams of lime several hours and distilled at 65°.

50 grams of potassium cyanide were added to the alcohol and refluxed on the steam-bath, the condenser being protected by a $CaCl_2$ tube. When it was nearly dissolved the solution was treated with the bromide warmed in order to prevent any unnecessary precipitation of the potassium cyanide. There was some precipitation, however. The rest of the potassium cyanide was added in two portions at intervals of 3-4 hours during the refluxing. The solution gradually darkened. At the end of ten hours the potassium bromide was filtered off and washed several times with absolute methyl alcohol. The washings were added to the filtrate, distilled from the steam-bath and the residue finally heated to 160° in a Wood's metal bath. It was then subjected to fractional vacuum distillation by the usual procedure.

First fractionation.

Fraction	Pressure	Temperature	Bath	Amount.
1	22 mm	70-95°	100-120°	125 grams
11	22 "	105-125°	120-140°	96 "
111	22 "	156-160°	170-180°	35 "

The distillation flask contained a dark viscuous residue which did not distill even when the bath was heated to 300° and the pressure reduced to 5 mm.

Second fractionation.

1	22 mm	66-75°	113 grams	$Br(CH_2)_3Br$
11	22 "	107-110°	100 "	$Br(CH_2)_3CN$
111	22 "	155° mainly	40 "	$CN(CH_2)_3CN$

Fraction 111 always contained a small amount of a white precipitate The yield was 42% calculated on the basis of the bromide which actually disappeared while 75% of the halide is accounted for.

The presence of potassium cyanide in the residue was shown by the Prussian blue test. The alcohol distillate has a strong isonitrile odor but in general it is not as marked as in the other method.

Method - 11.

The best result was obtained by mixing all the materials together and refluxing for 9-10 hours.

$Br(CH_2)_3Br$	750 grams.
KCN	240 "
CH_3OH	1000 cc

The quality of the chemicals was the same, except the potassium cyanide, which was Kahlbaum's " Zur analyse."

The potassium bromide precipitate gave a decided test for potassium cyanide as was expected.

Distillation.

Fraction	Pressure	Temperature	Bath	Amount	Substance
1	22 mm	65-90°	130°	260 g	$Br(CH_2)_3Br$
11	22 "	110-120°	135-165°	170 g	$Br(CH_2)_3CN$
111	26 "	140-163°		60 g	$CN(CH_2)_3CN$

In this case the yield is 45-50% calculated on the basis of the bromide which has disappeared but of course more of the bromide is recovered.

The best comparative study of the methods is seen in the following table. The numbers represent the percent of trimethylene bromide which has been converted into the product opposite to which they stand. Since this purpose of comparing the these results was not planned when some of these modifications were tried the relationships are not absolutely quantitative, but do point out the proper method of procedure.

Substance	Gabriel's Method	Method 1	Method 11
$Br(CH_2)_3Br$	27%	31%	31%
$CN(CH_2)_3CN$	15%	18%	16%
Recovered $Br(CH_2)_3Br$	8%	26%	35%
Total bromide accounted for	49%	75%	82%

Conclusion.

From these results it follows that the best method for making γ-bromobutyronitrile is by the use of methyl alcohol as a solvent and the use of an excess of trimethylene bromide over the potassium cyanide since the unchanged bromide is easily separated. The best results would probably be obtained by the procedure in method 11, but with a larger proportion of the bromide. The use of a soxhlet tube for the potassium cyanide might give even better satisfaction. The use of methyl alcohol as a solvent for making nitriles from potassium cyanide and a halide is suggested as a general method.

δ-Cyano- α-acetylvalerianic ethyl ester.

This substance is not described in the literature.

A study of the effects of varying the proportions of the reacting substances was made in this case also. It was formed by the action of γ-bromobutyronitrile on sodium acetoacetic ester using absolute ethyl alcohol as a solvent. The principal reactions are:

(1) $CH_3C(=O)CH_2.COC_2H_5 \rightleftharpoons CH_3C(OH)=CH.COC_2H_5$

(2) $CH_3C(OH)=CHC(=O).OC_2H_5 + NaOC_2H_5 \rightarrow CH_3C(ONa)=CH\,COC_2H_5 + C_2H_5OH$

(3) $CH_3C(=O)ONa = CH\ COOC_2H_5 + Br(CH_2)_3CN \rightarrow CH_3C(=O) - CH(CH_2CH_2CH_2CN)\ COOC_2H_5$

(4) $CH_3C(=O) - CH(CH_2CH_2CH_2CN)\ COOC_2H_5 \rightleftharpoons CH_3C(OH) = C(CH_2CH_2CH_2CN)\ COOC_2H_5$

(5) $CH_3C(OH) = C(CH_2CH_2CH_2CN)COOC_2H_5 + CH_3C(ONa) = CHCOOC_2H_5 \rightleftharpoons CH_3C(ONa) = C(CH_2CH_2CH_2CN)COOC_2H_5 + CH_3C(OH) = CH\ COOC_2H_5$

(6) $CH_3C(ONa) = CHCOOC_2H_5\ CH\ CH\ CH\ CN + Br(CH_2)CN \rightarrow CH_3C - C(CH_2CH_2CH_2CN)_2 - COOC_2H_5 + NaBr$

1,7-dicyano 4-aceto-
4 carboxethyl heptane.

From a consideration of these reactions it was predicted that equivalent proportions of acetoacetic ester, the nitrile, and sodium would result in the formation of 1,7-dicyano 4-aceto 4-carboxethyl heptane by equation (5) and (6) as well as the product desired δ-cyano-α-acetylvalerianic ethyl ester by equation (2), while an excess of acetoacetic ester over equivalent proportions of the nitrile and the sodium should displace the equilibrium, equation (4), to the left and favor the formation of the latter at at the expense of the former. Experiment confirms this.

Experiment 1.

Since, when this substance was made using equivalent quantities, it was not undertaken with this comparative study in mind the results are not as rigidly comparable as desired. In every case when these quantities were used there was considerable high boiling substances and the results checked roughly the following.

Materials.

γ-Promobutyronitrile, b.p. 95-115°/22 mm	65 grams
Acetoacetic ester	50 "
Sodium (clean and dry)	9 "
Absolute ethyl alcohol	125 cc

The nitrile was prepared previously as described. The acetoacetic ester was Kohlbaum's Fabrik. In order to be sure of the purity it was redistilled. The alcohol was freshly purified by refluxing twice for several hours over an excess of good lime. A little less than the calculated amount of acetoacetic ester and sodium were used in order to allow for a small amount of impurities in the nitrile.

The sodium was first dissolved in the alcohol in the usual manner. This required some warming. The solution was cooled and kept cool by surrounding with water. The ester was gradually added and then the nitrile. With a water cooled condenser protected by a $CaCl_2$ tube this was refluxed on the steam bath for 9.5 hours when the solution was found to be neutral to moist litmus. After filtering off the bromide and washing it with absolute alcohol the entire filtrate was distilled as completely as possible from the steam bath, and then heated to 200° in an oil bath. The small amount of bromide which precipitated was dissolved in 100 cc of water, the oily layer separated, the aqueous solution was extracted twice with ether and the whole in ether solution solution was dried over anhydrous sodium sulphate. After filtering off the sulphate the ether was evaporated giving 80 grams of an oily residue which is practically the calculated

amount. Fractional vacuum distillation gave the results in the following table.

Fraction	Pressure	Temperature	Path	Weight
1	760 mm	100°	200°	few drops
11	18 "	120-125°	170-185°	
111	5 "	125-165°	185-215°	11 grams
1V	5 "	160-170°	225-240°	25 "
V	5 "	180-200°	250-290°	5 "

Fraction 11 was mainly unchanged acetoacetic ester. The temperature rose gradually during the distillation of fraction 111, the contents of the flask turning very dark. That this fraction is δ-cyano-α-acetovalerianic ethyl ester is proven by its hydrolysis to δ-acetylvalerianic acid. V was mainly proven to be 1,7-dicyano 4-aceto 4-carboxthyl heptane as described later. Assuming 1V to contain all of the desired product the yield is 33% calculated on the basis of the sodium used. A refractionation would probably have increased the yield somewhat.

Experiment - 11.

The same proportions and the same quality of chemicals and the same procedure were used a second time.

γ-Bromobutyronitrile	60 grams
Sodium	8.5 "
Acetoacetic ester	48 "
Absolute alcohol	25 cc

The weight of the sodium bromide was 34 grams, the theoretical amount. It was found necessary to distill the product at a temperature as low as possible in order to prevent polymerization.

Fraction	Pressure	Temperature	Path	Amount
1	5 mm	60-160°	100-200°	
11	5 "	160-170°	220-235°	24 grams

Redistillation of fraction 1 gave but a few drops more of fraction 11. Again the yield is about 33%. From this it is evident that the yields by this method cannot exceed 30-40%.

Experiment - 111.

The next time 1 1/3 equivalents of acetoacetic ester were used to equivalent amounts of sodium and the nitrile. The data is tabulated below.

γ-Bromobutyronitrile	30 grams
Sodium	4.3 "
Absolute alcohol(ethyl)	65 cc
Acetoacetic ester (equivalent amount, 26.3 g)	35 grams

Distillation of products.

Fraction	Pressure	Temperature	Path	Amount
1	760 mm		200°	
11	5 "	80-120°	100-150°	
111	0.5 mm	120-140°	150-200°	few cc
1V	0.5 "	140-150°	200-210°	27 grams
V	0.5 "	150-200°		few drops
V1	0.5 "	200-205°	280-290°	" "

By fractionating 1V the yield is seen to be 73% on the basis of the sodium used. There was scarcely any of the higher boiling substance.

Experiment -1V.

One more run was made using 1.4 times the calculated amount of the ester.

γ-Bromobutyronitrile	140 grams
Acetoacetic ester (equivalent amt., 113 g)	160 "
Sodium	20 "
Absolute ethyl alcohol	300 cc

The weight of the sodium bromide precipitated was 87

grams almost equal to the calculated amount. This does not char when heated on the platinum foil. At the end of the refluxing the copper wire test showed no test for bromine. This product was fractionated more completely than the others.

First fractionation.

Fraction	Pressure	Temperature	Amount.
1	80 mm	40-50°	12 grams
11	80 "	110-112°	46 "
111	20 "	90-140°	33 "
	2 "	120-150°	
1V	2 "	150-160°	119 "

There was only a small amount of dark viscuous residue left in the distilling flask.

Since fraction 11 is probably almost pure acetoacetic ester the refractionation was begun with fraction 111 and carried out in the usual manner.

Second fractionation.

111	2-3 mm	70-150°	18 grams
1V	2 "	150-152°	128 " (δ-cyano- α-aceto-valerianic ester)

A small amount of dark viscuous residue was again left in the distilling flask. The yield in this case is seen to be 75% as compared to 30-40% when equivalent quantities of the initial materials are used.

Properties of δ-cyano- α-acetovalerianic ethyl ester.

Because of superheating it was found difficult to determine accurately the boiling point of this substance under diminished pressure. The most reliable value obtained was 154° under 2 mm pressure. When heated even under greatly reduced

pressure it turns dark and seems to polymerize gradually. The odor of the product obtained was unpleasant but this may be due to impurities. It is soluble in most organic solvents. The product obtained was clear and colorless.

Conclusion.

The advantage of an excess of acetoacetic ester for this case has been demonstrated by increasing the yield of the product from 30-40% to 75% and almost entirely eliminating side reactions. It may always be advantageous when it is desired to condense only one molecule of a substance with the acetoacetic ester molecule to use an excess of the ester providing it can be conveniently separated as in this case or if the halide is comparatively expensive.

1,7-Dicyano 4-aceto 4-carboxethyl heptane.
Di-(γ-cyano propyl)acetoacetic ethyl ester.

That fraction V of the distillation under method 1, page 58, is this substance has been established by the following procedure.

It was redistilled and gave a fraction practically constant at 200° under 5 mm pressure, bath 290°. The distillate was slightly yellow. By cooling and rubbing with a glass rod it was caused to crystallize slowly. This was washed with ether thoroughly and sucked dry on a filter. The product was colorless and crystalline with a pleasant nutty odor, m.p., 73.5°. A nitrogen determination by the Dumas method gave the following results:

	1	11
Weight of Substance	0.1842 g	0.1809 g
cc of gas	15.0	15.5
Temperature	24°	20°
Barometer	748 mm	743 mm
Temperature	20°	19°
Percent Nitrogen	9.1	9.5

Theoretical percent of Nitrogen.... 10.6

This is rather low but the nitrogen was evolved very slowly. In No.1, the combustion required such a long time that the $NaHCO_3$ was completely decomposed and in the second, the carbonate tube broke. A consideration of the possible products shows that this is sufficiently accurate to establish its identity.

This was further confirmed by hydrolysis. 1.3 gram of the substance was refluxed with constant boiling hydrochloric acid 6-7 hours. A gas was evolved which gave a precipitate which effeversced when treated with dilute acid, indicating a carboxethyl group. This was made alkaline with Na_2CO_3 and extracted once with benzene to remove any of the unchanged original material and once with a little ether; acidified with hydrochloric acid and extracted three times with ether, dried over anhydrous sodium sulphate and upon evaporation of the ether a small amount of a viscuous liquid which could not be made to crystallize, was obtained. This was placed in a vacuum desiccator over soda-lime for several days in order to remove any low boiling acid or moisture.

With constant boiling hydrochloric acid 1,7-dicyano 4-aceto 4-carboxethyl heptane should hydrolyze to δ-acetoazelaic acid, a substance which is not described in literature, but its neutrality equivalent is 115.05.

The product obtained in this hydrolysis was titrated

with standard alkali, N.F. = 0.0865

Weight of acid	0.1081 gram
No. cc of alkali	10.8
Neutrality equivalent	115.5

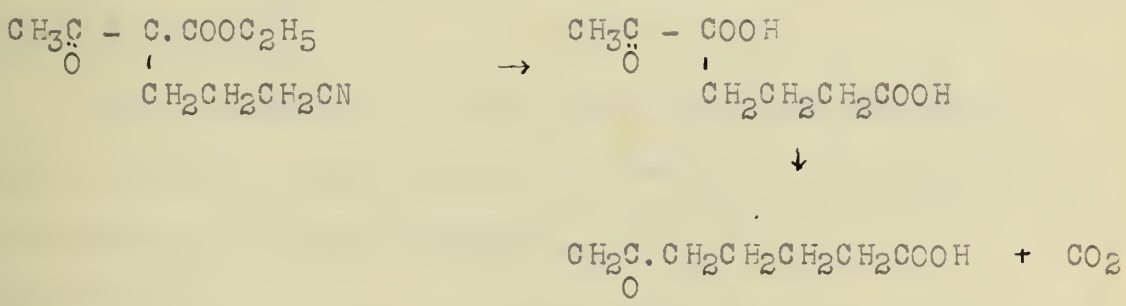
This agrees with the above value.

Properties of 1,7-Dicyano 4-aceto 4-carboxethyl heptane.

Boiling point approximately 200° under 5 mm pressure, bath 290°; melting point 73.5°; colorless with a pleasant odor. Almost insoluble in alcohol, ether, and carbon disulphide, chloroform, petroleum ether and water but readily soluble in benzene.

δ-Acetylvalerianic Acid.

δ-Cyano- α-acetovalerianic ester hydrolyzes almost quantitatively to δ-acetylvalerianic acid with constant boiling hydrochloric acid.



For this purpose the amounts used were generally in the ratio of about 20 grams of the acid to 100 cc of 20% hydrochloric acid. Although the ester went into solution inside of an hour the mixture was refluxed several hours longer. The solution becomes slightly colored. It was then neutralized with Na_2CO_3 and found to require only about 90% of the calculated amount showing

that some of the hrdrochloric acid had been volatilized as predicted due to a change in the nature of the solvent. If necessary more water was added to completely dissolve the salt. This solution was extracted with ether, in order to remove neutral substances, until a portion left no residue when dried with sodium sulphate and evaporated. It was next made distinctly acid to congo red by the addition of hydrochloric acid. If the proportions were just right a large portion of δ-acetylvalerianic acid formed an oily layer on the surface while the addition of an excess of acid caused this to disappear. If ether extraction alone were used it sometimes required 10-15 extracts since the acid is very soluble in water. The process was always tested for completion by drying the last portion with sodium sulphate and evaporating the ether. A method found to be more effecient was to assist by salting out with ammonium sulphate. The ether extract was dried with sodium sulphate, the ether evaporated and the residue distilled under low pressure.

That the product of this hydrolysis is δ-acetylvalerianic acid was established by titration with standard alkali and by analysis of its sodium salt.

Distillation.

It was desired to obtain this acid in a state of absolute purity for conductivity measurements. Towards this end it was first distilled under different pressures. A portion was fractionally distilled at a fraction of a millimeter pressure. It boiled constant at 135°, bath 195°. This was redistilled at 181-182° at 25 mm. bath 235°. During the distillation the flask

was inclined so that more of the condensate could run from the stoppers into the receiving flask. This latter bore the Jena brand. This acid always darkens slightly when heated leaving a little hight boiling residue. It was next converted into the sodium salt as described in the following section.

Preparation of the Sodium Salt of δ-Acetylvalerianic Acid.

Instead of making this salt in the usual manner by precipitation with sodium hydroxide dissolved in absolute alcohol it was made by equivalent amounts of metallic sodium dissolved in absolute alcohol. The advantages considered were the absence of water and greater ease of solution.

For this purpose 1.8 gram of sodium was dissolved in 100 cc of absolute alcohol then, 11.5 grams of the acid were added gradually to the hot solution. After refluxing a few minutes, the solution was complete. The addition of 100 cc more of absolute alcohol failed to dissolve a small amount of the substance. This was filtered off, washed with alcohol and dried in an oven at 80-90° for 2-3 hours. The addition of a little alcohol and concentrated sulphuric acid to a small portion produced an odor similar to that of ethyl benzoate. The analysis of this substance gave the following results.

Weight of substance	0.02505
Weight of sodium sulphate	0.01595
Percent of sodium	20.6

There was not enough for a duplicate analysis. The only substance which would have much possibility of being present, considering the reactions, giving a salt of this composition is α-acetyl-

adipic acid, $HOOC - CH.CH_2CH_2CH_2COOH$ (with $CH_3.C=O$ attached at the CH). The percent of sodium in the salt is 19.9. The presence of this was suspected previously as it seemed to lose CO_2 slowly.

The filtrate was clear and slightly acid to moist litmus. When cool the white precipitate completely filled the dish seeming to combine with the alcohol giving the consistency of ivory soap. With suction and much difficulty this was filtered through a Buchner funnel with a hardened filter paper and washed three times with absolute ether. The filtrate was concentrated and treated in the same manner, the precipitate being added to the other. The salt is very soluble, as a few cubic centimeters of filtrate remaining contained an appreciable amount. The alcohol was evaporated and the residue saved separately. This process was repeated with two more portions of alcohol of about the same volume. The second solution no longer reddened moist litmus. The centrifuge was also used for removing the solvent but the process was very slow.

The salt was dried in an electric oven at 90-100° for four hours, pulverized in an agate mortar, and then placed in an evacuated $CaCl_2$ desiccator over night. The product was white and fluffy. Its aqueous solution was slightly alkaline to litmus.

Analysis.

	I	II
Weight of salt	0.2055 gram	0.2137 gram
Weight of sodium sulphate	0.0879 "	0.0913 "
Percent of sodium	13.85	13.84

Theoretical percent of sodium.... 18.85

The method of analysis was that described in Treadwell-Hall Analytical Chemistry, vol. II. A large portion of the ammonium carbonate used was tested for volatility

Recovery of the Acid from the Salt.

15 grams of the salt were dissolved in 50 cc of water. For some unaccountable reason the solution was slightly colored. Keeping cool, 10 cc of hydrochloric acid (sp.g. 1.19, 37%) in an equal volume of water were added. Extracted twelve times with 20 cc of alcohol free ether. After drying with sodium sulphate, the evaporation of the twelth extracts showed the extraction to be complete. The ether solution was dried with sodium sulphate over night. After the evaporation of the ether and reduction of the pressure at the beginning of the distillation a few drops of water came over. This suggested the formation of a hydrate. During the second distillation a fraction boiling at 160° under 13 mm, bath 235°, was collected.

After cooling in an evacuated $CaCl_2$ desiccator it was pulverized in an agate mortar. The results of titrating this with standard alkali are given in the next section.

Titration with $Ba(OH)_2$ solution.

$Ba(OH)_2$ solution was used since it is very easy to prepare and keep free from CO_2. Phenolphthalein was used for the indicator. The acid was dissolved in hot conductivity water which had been boiled just previous to the titration. The determination was completedin the hot solution. At the same time the alkali was standardized against benzoic acid which had been recrystallized from water and alcohol twice, then distilled under vacuum as

described by G.W.Morey.[12]

Standardization.

	1	11
Weight of Benzoic acid	0.0940	0.1182
Cc of $Ba(OH)_2$ solution	54.05	68.10
Normality of $Ba(OH)_2$	0.01425	0.01424

In the following table are the results for the titration of the acid.

	1	11
Weight of Acid	0.1050	0.0869
Cc of $Ba(OH)_2$ solution	57.3	42.50
Neutrality equivalent	143.8	143.7

Calculated equivalent..... 144.1

Properties of δ-Acetylvalerianic Acid.

The acid purified in the above manner melts sharply at 36.5°. Here again because of superheating it was difficult to determine the boiling point accurately. They were found to be approximately 135° 0 mm, bath 195° and 181° at 25 mm, bath 235°. The ionization constant of the above product has not been determined because it has been impossible to obtain water of the necessary purity since it was obtained. However the constant has been found to be close to 1.93×10^{-5} as shown later. As previously observed this acid was found to hygroscopic.

IX - Experimental.

B. Conductance.

B - Conductivity Measurements.

Method.

The Kohlraucsh method[1] was used for the conductance measurements.

1 - Apparatus.

Constant Temperature Bath.[2]

For maintaining constant temperature of the solution during the measurements a bath composed of a six liter Dewar flask containing water, surrounded by a somewhat larger glass vessel covered with asbestos paper was used as previously. The stirrer was run by a small electric motor instead of the water motor previously used in the laboratory. In order to maintain the most constant temperature it was found best to keep the room temperature just below 25°, then the temperature of the bath could be raised if necessary by means of the nichrome coil heater. The thermometer was calibrated by the U.S. Bureau of Standards and was graduated to 0.05°, so it was easily possible to read it to 0.01°. The readings were made at 25° ± 0.01°.

Bridge and Resistance Box.

The bridge was of the drum type manufactured by the Leeds-Northrup Co. Decade' resistance boxes were used. The calibration of these have been carefully made and recorded previously.[3] This calibration has been checked from time to time. Readings were always taken as near to the center of the bridge as was possible since the chance for error is less.

Current.

In order to prevent polarization a direct current generated by dry cells was changed into an alternating one by means of a small induction coil, with buzzer attached for producing a high pitched tone. In the circuit, a carbon rheostat was inserted. By regulating this and the pitch of the tone of the buzzer it was possible to obtain a distinct tone minimum. The current was never allowed to pass through the solution longer than necessary because of the heating and decomposition of the solution.

The Telephone.

This is the Paul instrument manufactured by R. W. Paul of New Southgate, London, the value of which for this work has been demonstrated by E. W. Washburn and his students.[4]

Weights.

These were calibrated accurately but the weighings were usually made in such a manner that it was not necessary to make the corrections. During two successive weighings of a substance the large w ights were not changed since the corrections were large. Since an accuracy of one tenth of one percent was sufficient, the error due to the smaller weights was not this large when 0.1 g of substance was weighed.

Conductivity Cells.

For the following measurements one cell was used for measuring the water and another for measuring the acid and salt. The water cell is much larger than the other and the

electrodes were also larger in order to give a sharper tone minimum. The electrodes of the smaller one were platinized in order to reduce polarization and to enable a more accurate reading to be made. Both were of the pipette type.

The cells were filled by drawing the liquid into it with the breath through a rubber tubing. In order to prevent CO_2 and other gases from going into the cell when filling and emptying a soda-lime tube was placed in the rubber tubing.

Glass Apparatus.

All glass apparatus was of good Jena glass and has been in use for this purpose in this laboratory and in contact with water for several years. The flasks used for making the dilutions were usually steamed out just before use each time. Well steamed tin foil was used for closing the mouth of the flask.

2 - Preparation of Conductivity Water.

The still used is composed of a large copper body of about 32 liters capacity supplied with a steam heating coil and a tin delivery tube cooled by means of running water.

This was filled with ordinary distilled water, 150 cc of alkaline permanganate solution added, and heated to boiling. The permanganate solution was made from the following proportions 6 gms. $KMnO_4$, 100 gms. KOH, and 1000 cc of distilled water. After standing several hours this was distilled and collected in glass bottles which have been in use for several years. During the distillation it was found necessary to keep a steady

current of steam issuing from the neck of the bottle. If this is too slow the water may be contaminated by laboratory fumes while if it is too fast it may sputter and injure the quality of the water. The first few liters were always discarded since they contain ammonia. When the bottles were filled the necks were covered with well steamed tin foil and inverted beakers and allowed to cool.

The body of the still contains an outlet near the top which should always be left open when not in use in order to prevent the possibility of its accidental filling and running over. If this occurs the delivery tube is contaminated and requires a thorough steaming before further use.

With this apparatus, when properly handled, there is but little trouble in obtaining, regularly, water of specific conductivity of 0.5-0.7 x 10^{-6} reciprocal ohms. It gradually deteriorates on standing several days.

3 - Water Correction.

The correction for the specific conductivity of water has been a matter of considerable difference among investigators. Kendall[5] showed that the best values of the ionization constants of acetic acid were obtained by neglecting this factor if the specific conductivity of the water is less than 0.9 x 10^{-6}. Derick[6] has also shown that the criterion "Calculated Λ_o" proves that this correction should not be applied in this case. Derick and Brady[7] have applied the criterion to the other members of the series of keto monobasic paraffin acids and found that the

correction should not be made if the specific conductivity of the water is 0.5-0.7 x 10^{-6}. The kind and not the amount of impurity seems to be the determining factor. Brady[7] has considered this question in detail. In the light of the above considerations the correction was not made to the conductance of the acid.

On the other hand, there is a general agreement that the correction should be applied to the conductance of the salt.

4 - Preparation of Solutions and Procedure of Measurements.

The solutions were prepared on the basis of an equivalent weight in 1000 grams of solution. Of course strictly they should be volume standard since the unit of conductance is defined on the volume standard but practically this will introduce an inappreciable error because of the extreme dilution of the solutions. That this is true has been shown by all the other acids of this series.[7]

The measurements were begun on the 0.02 N solutions, since the mass law generally deviates above this concentration. At this concentration a convenient amount of material could be weighed without small errors in weighing affecting the results beyond the desired accuracy. Enough of the substnace was weighed out to make up 300-400 grams of solution. Both acid and salt were weighed by means of an ordinary weighing tube. If the fingers were kept clean and dry it was found they could be used without covering for handling this and obtain the necessary accuracy. Care was always taken to allow the balance and tube

to come to equilibrium before the final weight was taken. This sometimes required nearly an hour. The method of using the weights is described under the section on weights. Since the acid was hygroscopic it was never poured into a wet flask and it was exposed to the air as briefly as possible. The solutions were weighed on a large balance to the accuracy of 0.05 gram. The flasks were all weighed and marked previously to the same point of accuracy.

Duplicate solutions were always prepared and dilutions made on each. If two solutions failed to check, another one was made from a previous concentration until a check of at least 0.1% was obtained for the bridge reading. Before the measurements on each dilution the cell was carefully rinsed with some of the solution to be measured. For this purpose 2-3 separate portions when properly used were usually sufficient. It was filled completely. Before the final reading of the bridge was made in each case at least two successive readings were found to check. A small difference in temperature makes a comparatively large difference in the resistance of the solution. On each dilution of each series the bridge was read with three different resistances. The box was plugged so as to bring the reading as near to the center of the bridge as possible.

In making a given solution the first portion of water may be poured directly from the bottle and the last may be removed with a pipette for the purpose of adding the last few cubic centimeters to the flask. Obviously the pipette should be carefully handled to prevent contamination of the water.

5 - Conductance Measurements and Ionization Constant of δ-Acetylvalerianic Acid.

Several series of conductance measurements were made on this acid, prepared at different times. Although the duplicates for each preparation usually checked with the desired accuracy for all dilutions, the measurements on the higher dilutions never quite checked for the acid prepared at different times. Furthermore, deviations in the ionization constant became greater after 0.001 N solution. In every case there was a small but gradual drop in this value to the 0.0001 N solution. This suggests that there may be a small amount of impurity present in slightly different proportions in each preparation. In order to determine if this is the source of the deviation, the pure acid has been prepared from the recrystallization of the sodium salt and its purity carefully determined as previously described. Because of the impossibility of obtaining water of the necessary purity recently these measurements have not yet been made. The following measurements were made on a fraction of the acid boiling constant at 162°(uncorr.) under 15 mm pressure. Although it is possible that this may form a constant boiling mixture with some impurity its previous distillation under slightly different pressures at practically constant temperature indicates that the amount of impurity is not large. Of course this procedure might not show the presence of a small amount of impurities because of the tendency to superheat and the short range of pressure. Distillation under higher pressures were feared because of decomposition. The following measurements show this gradual drop

in the ionization constant. No conclusion as to the cause can be made with any degree of certainty until measurements have been made on the pure acid which is on hand.

Strength of Solutions.

Table IX

Wt. Acid	Wt. Solution	Normality	Wt. Acid	Wt. Sol.
0.7037	244.2	0.02000	0.9380	323.4
Wt. Solution	Wt. of H_2O	0.01000	Wt. Sol.	Wt. H_2O
150	150	0.01000	150	150
225	75	0.00750	225	75
200	100	0.00500	200	100
150	150	0.00250	150	150
120	180	0.00100	120	180
225	75	0.00075	225	75
200	100	0.00050	200	100
150	150	0.00025	150	150
120	180	0.00010	120	180

Table X

	Bridge Reading A	Bridge Reading B	Box Reading
0.020			
	5305	5307	240
	5205	5205	250
	5108	5106	260
0.010			
	5170	5170	360
	5102	5103	370
	5033	5036	380
0.0075			
	5090	5090	430
	5033	5032	440
	4978	4977	450
0.0050			
	5000	5000	550
	4957	4953	560
	4909	4908	570
0.0025			
	5408	5407	670
	5370	5372	680
	5332	5333	690

Table X (con't)

	Bridge Reading A	Bridge Reading B	Box Reading.
0.00100			
	5170	5170	1200
	4972	4972	1300
	4987	4987	1400
0.00075			
	5365	5365	1300
	5178	5178	1400
	5008	5008	1500
0.00050			
	5258	5253	1700
	5115	5108	1800
	4980	4975	1900
0.00025			
	5360	5360	2400
	5255	5255	2500
	5160	5155	2600
0.00010			
	5420	5430	4000
	5355	5370	4100
	5295	5305	4200

Table XI

$L_{H_2O} = 0.6 \times 10^{-6}$

Temperature = $25^{\circ} \pm 0.01^{\circ}$

Cell Constant 0.06233 $\Lambda_{\infty} = 376$

Concentration	Λ_{μ}	$K_{\mu} \times 10^{-5}$
0.02000	11.49	1.926
0.01000	16.14	1.924
0.00750	18.63	1.947
0.00500	22.66	1.933
0.00250	31.60	1.928
0.00100	48.49	1.910
0.00075	55.22	1.896
0.00050	66.31	1.882
0.00025	90.00	1.883
0.00010	131.40	1.879

The values of Λ above were calculated from the average of the two resistances.

6 - Equivalent Conductance at Infinite Dilution.

By the use of the Ostwald[8] method Λ_o was calculated to be 376. Conductance measurements on the sodium salt gave the same value. For this purpose a series of conductance measurements were made on a series of dilution and from the results Λ_o was obtained by two different methods of plotting. In the one case $\frac{1}{\Lambda}$ was plotted against $(C\Lambda)^{0.45}$[9] and in the other Λ against $\sqrt[3]{C}$.[10] By extropolating a straight line through the points for the salt was found to be 80.

The value $\Lambda_{ona^+} = 51.2$ and $\Lambda_{ona^+} = 347.2$ at 25° were chosen for calculating Λ_o for the acid.

$$\Lambda^{o}_{Acid} = \Lambda^{o}_{Salt^-} - \Lambda^{o}_{Na^+} + \Lambda^{o}_{H^+}$$

$$\Lambda^{o}_{Acid} = 80 - 51.2 + 347.2 = 376.$$

7 - Conductance Measurements on the Sodium Salt of δ-Acetylvalerianic Acid.

For this purpose the salt was prepared and found to be pure by analysis as previously described. This method is usually used in this laboratory rather than the titration method as it furnishes a check on the purity of the acid. The procedure was the same for the acid.

0.01 N Solution.

0.5074	Wt. of Salt	0.4395
305.5	Grams of Solution	264.6

The dilutions were the same as for the acid.

Table X 11

	Bridge Reading A	Bridge Reading B	Box Reading
0.01000			
	5043	5043	93
	4988	4988	95
	4938	4938	97
0.00750			
	5088	5092	120
	4967	4970	125
	4888	4892	130
0.00500			
	With this dilution a new cell was used.		
	5135	5135	115
	5030	5030	120
	4930	4928	125
0.00250			
	5077	5080	340
	5006	5007	350
	4935	4936	360
0.00100			
	5070	5072	830
	5013	5013	850
	4927	4927	880
0.00075			
	5060	5062	1100
	4992	4995	1130
	4924	4932	1160
0.00050			
	5088	5088	1600
	5040	5013	1650
	4935	4943	1700
0.00025			
	5075	5100	3100
	4995	5018	3200
	4917	4945	3300
0.00010			
	5125	5150	7000
	5015	5050	7300
	4912	4956	7600

Conductance of Sodium Salt at 25°

$L_{H_2O} = 0.962 \times 10^{-5}$

Cell Constant.

For conc. 0.01 and 0.0075 = 0.06776

For conc 0.0075-0.0001 = 0.06614

Table XIII

Normality	L_c	Λ_c
0.01000	0.0007155	71.55

Table XIII (con't)

Normality	$\perp c$	Λc
0.00750	0.0005433	72.44
0.00500	0.0003673	73.46
0.00250	0.0001876	75.06
0.00100	0.00007645	76.45
0.00075	0.00005774	76.98
0.00050	0.00003896	77.92
0.00025	0.00001955	78.20
0.00010	0.000008037	80.37
0.00010	0.000007929	79.29

Since there were deviations in the bridge readings of the last two dilutions they are calculated separately.

Table XIV

Normality	$1/\Lambda_{\sim}$	$(c\Lambda)^{0.45}$	$\sqrt[3]{c}$
0.01000	0.01397	0.8601	0.2154
0.00750	0.01380	0.7599	0.1957
0.00500	0.01361	0.6372	0.1710
0.00250	0.01332	0.4710	0.1357
0.00100	0.01308	0.3144	0.1000
0.00075	0.01299	0.2771	0.09085
0.00050	0.01283	0.2382	0.07937
0.00025	0.01278	0.1703	0.
0.00010	0.01244	0.1141	0.04642
0.00010	0.01261	0.1134	

The plot of these values was not inserted here because of the necessary large size required for obtaining Λ_o to the desired accuracy.

7 - The Criterion "Calculated Λ_o" Applied to the Conductance Data of δ-Acetylvalerianic Acid.

Derick[11] has shown that "Calculated Λ_o" is much more sensitive to errors than the ionization constant and therefore can be used to advantage in detecting the presence and nature of these. If the mass law holds for a given acid the value of the expression at two different concentrations will be identical from which it follows that,

$$\Lambda_o = \frac{\Lambda \Lambda_1 (c\Lambda - c_1\Lambda_1)}{c\Lambda_1^2 - c_1\Lambda_1^2}$$

" Calculated Λ_o" for δ-acetylvalerianic acid. The values for Λ are found in the table XIII.

Table V

Concentration		$\Lambda_{o,c}$
0.02000 and	0.01000	369
	0.00750	517
	0.00500	419
	0.00250	381
	0.00100	350
	0.00075	337
	0.00050	339
	0.00025	378
	0.00010	356
0.01000 and	0.00750	2250
	0.00500	464
	0.00250	385
	0.00100	348
	0.00075	336
	0.00050	331
	0.00025	347
	0.00010	358
0.00750 and	0.00500	319
	0.00250	337
	0.00100	321
	0.00075	320
	0.00050	318
	0.00025	340
	0.00010	354

Table V (con't)

Concentration	$\Lambda_{o\,\omega}$
0.00500 and 0.00250	345
0.00100	330
0.00075	320
0.00050	320
0.00025	341
0.00010	355.

These calculations show that there is some error present. The deviations are not as large as they seem at first glance since this criterion is so sensitive. The use of $\Lambda_1 = 18.58$ instead of 18.63 for $C_1 = 0.0075$ with $C = 0.01$, $\Lambda = 16.14$ gives $\Lambda_o = 413$ instead of 2250. In this case a difference of 0.25% in Λ makes a 500% change in "Calculated Λ_o". The value for $\Lambda_1 = 18.58$ was obtained from another series. Since 18.63 was obtained in several other independent measurements it was used here. Derick[11] has shown that in cases where a fairly good series of ionization constants is obtained for different dilution the deviations in "Calculated Λ_o" may be enormous.

The "Calculated Λ_o" for the concentrations 0.02 and 0.0075, the 0.01 and 0.0075 and the 0.0075 and 0.0050 indicates the 0.0075 to be in error for some reason, even if check results for $\Lambda_1 = 18.63$, $C_1 = 0.0075$ were obtained.

It will be observed that most of the results are between 320 and 350. This indicated constant error. Measurements on different preparations of the acid always gave low results. This suggests that the error is probably not due to technique but is due either to the impurity of the acid or to some reaction in solution. It will be necessary to make measurements on the acid

which is now known to be pure before deciding this.

8 - The Effect of Frrors in Λ , Bridge Reading, Resistance Box and Λ_o on the ionization Constant.

Derick[11] has pointed out from a consideration of the expression, $$\frac{dk}{k} = \frac{2\Lambda_o - \Lambda}{\Lambda_o - \Lambda}\left(\frac{d\Lambda}{\Lambda} - \frac{d\Lambda_o}{\Lambda_o}\right),$$

that the ionization constant is affected less by errors in and $\Lambda + \Lambda_o$ in the more concentrated solutions where the mass law holds, since $\frac{dk}{k} = 2\left(\frac{d\Lambda}{\Lambda} - \frac{d\Lambda_o}{\Lambda_o}\right)$ as a limit for concentrated solutions and,

$$\frac{dk}{k} = \infty\left(\frac{d\Lambda}{\Lambda} - \frac{d\Lambda_o}{\Lambda_o}\right)$$

as a limit for dilute solutions.

A consideration of this equation for practical purposes is useful. The data for δ-acetylvalerianic acid will give about the same results as any weak acid. Assume first that the correct Λ_o is used and it is desired to know how K varies with errors in Λ . Then,

$$\frac{dk}{k} = \frac{2\Lambda_o - \Lambda}{\Lambda_o - \Lambda}\left(\frac{d\Lambda}{\Lambda}\right)$$

For 0.02 N solution,

$$\frac{dk}{k} = \frac{(752 - 11)}{(376 - 11)} = 2\ \frac{d\Lambda}{\Lambda}$$

For 0.00010 N solution,

$$\frac{dk}{k} = \frac{(752 - 130)}{(376 - 130)} = 2.5\ \frac{d\Lambda}{\Lambda}$$

From this it is obvious that an error in Λ will produce an error from 2 to 2.5 times as great in (k) depending on the concentration.

tration.

But errors in Λ will be due to impurities or to errors in reading the bridge, assuming it to be calibrated correctly. It is not possible to determine in general how impurities affect Λ by this method. In this case we have

$$\frac{dk}{k} = \frac{dc}{c} + \frac{2\Lambda_0 - \Lambda}{\Lambda_0 - \Lambda}\left(\frac{d\Lambda}{\Lambda}\right)$$

The effect of an error in reading the bridge on Λ can be calculated definitely. It is easily shown that,

$$\Lambda = \frac{1000\ k}{cR}\left(\frac{1000 - a}{a}\right)$$

K = Cell constant
c = Concentration of electrolyte
R = Box resistance
a = Bridge reading.

From this it follows that,

$$\frac{d\Lambda}{\Lambda} = -\frac{1000}{1000 - a}\left(\frac{da}{a}\right).$$

Since the readings are always made near the center of the bridge,

$$\frac{d\Lambda}{\Lambda} = -2\left(\frac{da}{a}\right)$$

From this the effect of errors on the ionization constant is seen. For 0.02 N solution,

$$\frac{dk}{k} = 2\left(\frac{d\Lambda}{\Lambda}\right) = -4\left(\frac{da}{a}\right).$$

For 0.0001 N solution,

$$\frac{dk}{k} = 2.5\left(\frac{d\Lambda}{\Lambda}\right) = -5\left(\frac{da}{a}\right)$$

From this it follows that an error of 0.10% in the bridge reading will produce one of 0.4-0.5% in the ionization constant.. The necessity for accurate and repeated reading of

each concentration is obvious if variations not greater than 0.1% are desired.

Errors in the calibration of the resistance box are seen to produce the same percent error in (k) but opposite in sign.

$$\frac{dk}{k} = - \frac{dR}{R}$$

If we assume that the wrong value for Λ_o has been chosen there results,

$$\frac{dk}{k} = -\left(\frac{2\Lambda_o - \Lambda}{\Lambda_o - \Lambda}\right) \frac{d\Lambda_o}{\Lambda_o}$$

For 0.02 N solution,

$$\frac{dk}{k} = -2 \frac{d\Lambda_o}{\Lambda_o}$$

For 0.0001 N solution,

$$\frac{dk}{k} = 2.5 \frac{d\Lambda_o}{d\Lambda_o}$$

From a consideration of these two formulae it follows that our error of 1.00% in the value for Λ_o will produce an error of 2% in the ionization constant at 0.02 N and one of 2.5% at 0.0001 N. Not only will the wrong value for the ionization constant be obtained but for the series of dilutions 0.02 to 0.0001 it will vary 0.5%, Λ_o must be known to an accuracy of 0.2% if all the values of (k) calculated for this series are to check within 0.10%. The conclusion to be drawn is that even if there is no error in the conductance measurements and if there are no impurities present (k) will gradually vary with each succeeding dilution, if the wrong value for Λ_o is chosen. For organic acids if Λ_o is known to an accuracy of 0.5 to 1 unit, the vlaue of (k) for the different dilutions should not vary more than 0.1 %.

X - XI. General Conclusion

and

Summary

X - General Conclusion.

From the considerations of a rather general survey of the field certain rather definite conclusions can be drawn but the problem is far from being completely solved. We know that the course of chemical reactions is conditioned by the nature and the position of substituents in the molecule. Again, the nature of a given substituent is modified by the nature and position of the other substituents so that in many cases the problem becomes exceedingly complicated. Derick considers that the best manner in which to begin the solution of such a perplexing situation is to determine the effect of the nature and position of a single substituent at a time, in as simple a molecule as possible, upon the tendency of a given atom to enter into a chenical reaction. For this purpose he has chosen to measure the effect of different substituents in the same position and the same substituent in different position upon the tendency of the carboxyl hydrogen to enter into the reaction ionization as measured by the free energy of the process. Several strongly negative radicals have been found to act uniformly in all cases. Their effects have been found to decrease in each successive position out the carbon chain to the η position for O= and to the epsilon position for several others. For the reaction ionization then the influence is in the order, 1-2-3-4-5-6-7-8-9-10, as suggested by Derick and not 1-2-3-5-6-4-(9-10-11)8 as claimed by Michael.

It is possible that this order may not hold for other reactions but it has been proven experimentally for one

reaction. Michael's scale of influence has not been proven experimentally for any reaction. His scale is complicated by the unfortunate choice of substituents, the polarity which is so uncertain.

XI - Summary.

1. Considerations have been given to the nature and measurements of chemical affinity and its relationship to chemical composition, constitution, space configuration, valence and the course of chemical reactions.
2. A new method of measuring polarity has been developed.
3. In conjunction with Derick and Brady tthe scale of influence for the effect of oxygen in the keto monobasic paraffin acids upon the tendency of the carboxyl hydrogen to ionize has been determined experimentally. It has been found that the order 1-2-3-5-6-4-7-(9-10-11)8 given by Michael is inaccurate while that suggested by Derick, 1-2-3-4-5-6-7-8-9-10 has been confirmed.
4. δ-Acetylvalerianic acid has been prepared by a new and efficient method. It has been obtained in a pure state for the first time and its ionization constant determined.
5. An efficient method for making trimethylene bromide from trimethylene glycol and aqueous HBr has been developed. By properly regulating the proportions the yield was increased over 30%. 80% of the glycol was converted into the bromide.
6. Absolute methyl alcohol was used as a solvent for making γ-bromobutyronitrile from trimethylene bromide and KCN. The yield with the usual solvent, a mixture of water and ethyl alcohol was 20-30% while with methyl alcohol it was 40-50%. This is suggested as a general solvent for making nitriles by this method.

7. For making δ-cyano-α-acetovalerianic ester, when an amount of acetoacetic ester equivalent to that of the bromide was used the yield was 30-40% while with 1.4 equivalents of the ester it was 75%. That the principal side reaction produced 1,7,-dicyano 4-aceto 4-carboxethyl heptane was demonstrated and that this was practically prevented in the latter case, proven.

8. Two new substances, δ-cyano-α-aceto valerianic ethyl ester and 1,7-dicyano 4-aceto 4-carboxethyl heptane have been made and characterized.

9. A preliminary study on a practical laboratory method for determining boiling points and standardizing thermometers has been made. It was shown to have a reproducibility of 0.1° for water.

10. Formulae showing the effect of errors in Λ, Λ_o, the bridge reading and the box resistance upon the ionization constant are given.

XII - Bibliography.

Bibliography.

11 - Chemical Affintiy.- Its nature and measurement.

1. Sackur- Die Chemische Affinitat und ihre Messung. Die Wissenschaft Sammlung naturwissenschaftlicher und mathemathi - sher Monographen, Heft, 24.

J. Campbell Brown - A History of Chemistry.
Patterson Muir- A History of Chemical Theories and Laws.
Kopp- Geschichte der Chemie.
Nernst- Theoretical Chemistry.
Mellor- Chemical Statics and Dynamics.
Partington- A Text-book of Thermodynamics.

2. Kopp- Geschichte der Chemie 2, 296.
3. " " " " 2,301.
4. " " " " 2, 299.
5. Sackur- Die Chenische Affinitat und ihre Messung, p.3
6. Bertholet- Recherches sur les Lois de l'affinite 1779. Ostwald Klassiker der exakten naturwissenschaften, No. 14.
7. Guldberg and Waage- Untersuchung uber die Chemischen Affinitaten. Ostwald Classiker der Exakten Wissenschaften.
8. Lowenthal and Lessen- J. prakt. Chem. 85, 321,401,(1862).
9. Ostwald, J. prakt. Chem. (2) 29 , 385,(1884).
10. Ostwald, J prakt. Chem. (2) 28, 449,(1883).
11. Warder, Ann.Chem. Jour, 3, 340,(1882)
12. Reicher, Ann. 228, 257, (1885).
13. Thompsen, Pogg. Ann. 138, 65,
14. Ostwald, J. prakt. Chem. (2) 16, 385; 18, 328; 19,468; 25, 1. Wied, Ann. 2, 429-671.
15. Berzelius, Ostwald's Klassiker der Exakten Wissenschaften No. 35, S. 168.
16. Mitcherlich, Lehrbuch der Chemie, 4 Aufl.
17. Nernst, Theoretical Chemistry, p. 656, Translation of 6th German Edition.
18. Nersnt, " " p, 708 " " "
19. Van't Hoff, Zeit. physik. Chem. 3, 608,(1889).

111 - Chemical Affinity and Composition.

1. Van't Hoff, Lectures on Theoretical and Physical Chemistry, part 111, pp. 113-143.
2. Claus, Ber. 14, 432, (1881).
3. Werner, Chem. News, 96,131,(1907).
4. Ostwald, Z. physik. Chem. 3, 190-197, 241-288,369-422,(1889)
5. See section on "the measurement of chemical affinity."
6. Vorlander, Ann. 320, 110,)1904)
7. Abegg, Z. Anorg. Chem. 39, 330,(1904)
8. Flursheim, J. prakt. Chem.(2) 71, 500,(1905). 76, 200,(1907). Ber. 29, 2016,(1906) J.Chem.Soc. 95,718,(1909)

9. Bauer, Ber, 37, 3317, (1904).
10. Klages, Ber. 37,924, (1904).
11. Michael, J.prakt. Chem. 60, 286,292,(1899).
12. 46, 205,345.
Ber. 39, 2138,(1906).
J.Am.Ch.Soc. 32, 999,(1910).
Ann. 363,21, (1908).
Am.Chem.J. 41, 119,(1909).
12. Markownikoff, Ann, 146, 344,153,255,(1870).
13. Hibbert, J.Chem. Soc.Proc. 25, 57, (1909).
14. Derick, J.Am.Ch.Soc. 33, 1152-1162,1167-1181,(1911).
15. " " " " " " 1156,1161,(1911).
16. Brooks, J.Am.Ch.Soc. 34, 495, (1912).

lV- Chemical Affinity and Constitution.

1. Menschutkin, Ann.chim.phys.(5) 20, 289-362, (1880).
23, 14-85, (1881)
30, 81-144,(1888).
2. Van't Hoff, Lectures on Theoretical and Physical Chemistry
111. 113-143.
Ansichten uber die Organischen Chemie, 1,284-285;
11, 252-254.
3. Ostwald, Z.physik Chem. 3, (1889).
4. Fichter and Pfister, Ann. 334, 201, (1904).
5. Ostwald, Z.physik. Chem. 5, 399,(1890); 6, 311,(1890).
6. Sudborough and Thomas, Trans, J.Chem. Soc. 97, 715,(1910).
7. Derick and Kamm, Ph. D Thesis, 1915, Univ. of Illinois.
8. Hinrichsen, Ann.336, 174, (1904).
9. Michael, J. prakt.Chem. 60, 467, (1899).
10. Stewart, Recent Advances in Organic Chenistry.
11. Flursheim, J.Chem Soc. 95, 718, (1909).
12. Michael, J.Am.Ch.Soc. 32, 990,(1910).
J.prakt. Chem.(2) 60, 331.
Ber. 39, 2138,2780.
" 40, 141.
13. Master's Thesis.
14. Derick, J.Am.Ch.Soc. 33,1167-1181(1911).
15. " " 34, 74-82,(1912).
16. " " 32, 1333, 1339,(1910).
17. " " 35, 1269, (1913).
18. Roth and Stroemer, Ber. 46, 262, (1913).
19. Henrich, Theorem der Organischen Chemie, Zweite auf. S. 344.

V- Chemical Affinity and Spcae Configuration.

1. Ostwald, Z. physik. Chem. 3, 241-88; 369-422,(1889)
2. " " " " 9, 553, (1892).
3. " " " " 5, 385-422,(1890).

Vl- Chemical Affinity and Valence.

1. Cohen, Organic Chem. 11, page 1.
2. Michael, J.prakt.Chem. 60, 295,(1899).

V11- Correlation of Affinity and Constitution.

1. Ostwald, Z. physik. Chem. 3, 170, 369-422, (1889).
2. Bethman " " " 5, 383-422(1890).
3. Holleman and deBrun, Rec. Tran.Chim 11, 20,360-364,(1901).
4. Wegscheider, Monats. 16, 153-158,(1895).
23, 287,-316,(1902).
26, 1265 (1905).
5. Bredig,Z. physik. Chem. 13, 289, (1894).
6. J.Am.Ch.Soc. 33, 1181-89,(1911).
Derick 34, 74,(1912).

V111- Theoretical Treatment of the Results of the Present Measurements.

1. Van't Hoff, Z. physik. Chem. 3, 608, (1889).
2. Derick, J.Am.Ch.Soc. 33, 1174, (1911).
3. Derick and Brady, Ph.D. Thesis, 1916, Univ. of Illinois.
4. " " " " " " " "
5. Colorimetric, Z.Biochem. 15,105-113, (1908).

1X- Experimental.- A. Synthetical.

1. W.H.Perkin, J.Chem.Soc. 57, 230,(1890).
2. Ficher and Gully, Ber, 30, 2047,(1897).
3. Wallach, Ann. 329,377,(1903).
4. " " 359,309,(1908).
5. Blaise and Koehler, Compt. rend. 148, 490, (1909).
6. Rebaul, " " 74, 613.
76, 1270
7. Germont, Ann. 158, 370, (1871).
8. Erlenmeyer, Ann. 197, 169-185,(1879).
9. Freund, Monats. 2,639,(1881).
10. Gustaveson, J.prakt. Chem. 59,304, (1899).
11. Gabriel, Ber. 22,3336.
12. Morey, J.Am.Ch.Soc. 34,1027,(1912).

X- Experimental.- B. Conductance.

1. Kohlrausch and Holborn, Leitsvermogen der Electrolyte, 1898.
2. Derick and Brady, Ph.D. Thesis, 1916.
" " Prasil, B.S. Thesis, 1914, Univ. of Illinois.
3. " " " " " " " " "
4. Washburn, not yet published.
5. Kendall, J.Chem.Soc. 101, 1283, (1912).
6. Derick, J.Am.Ch.Soc. 36, 228, (1914).
7. Derick and Brady, Ph.D. Thesis, 1916.
8. Ostwald, Affinitatmessung an Schwachen Sauren und Basen, p 9
9. A.A.Noyes, J.Am.Ch.Soc.
10. Kohlrausch and Holborn, Leitvermogen der Electrolyte, pp.107-110.
11. Derick, J.Am.Ch. Soc. 36, 2268-2283,(1914).

Biography

The early education of the writer was received from the schools of Plover, Iowa, graduating from the High School of that place in 1908. The A.B. degree was received from Morningside College in 1912. During his undergraduate work a major in chemistry was taken. In the summer of 1912 he entered the Graduate School of the University of Illinois and received the M.A. degree in chemistry in 1914 and has since been continuing his graduate work here.

For the year 1912-1913 he was graduate assistant in chemistry and since that time has been assistant in chemistry at the University of Illinois. During the Summers of 1914 and 1915 he was engaged in the organic synthetical work for the University. He is a member of the Sigma Xi, Phi Lambda Upsilon Alpha Chi Sigma and the American Chemical Society.

UNIVERSITY OF ILLINOIS-URBANA
3 0112 082198620